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1. Slama TG, Sklar SJ, Misinski J, et al: Randomized comparison of cefamandole, cefazolin, and cefuroxime prophylaxis in open-heart surgery. *Antimicrob Agents Chemother* 1986;29:744-747.
2. Haley RW, White JW, Culver DH, et al: The financial incentive for hospitals to prevent nosocomial infections under the prospective payment system. *JAMA* 1987;257:1611-1614.

Please consult Brief Summary of Prescribing Information on next page before prescribing or administering ZINACEF.

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Brief summary. Before prescribing, consult complete Prescribing Information.

INDICATIONS AND USAGE: ZINACEF® is indicated for the treatment of patients with infections caused by susceptible strains of the designated organisms in the following diseases:

1. **Lower Respiratory Tract Infections,** including pneumonia, caused by *S pneumoniae* (formerly *D pneumoniae*), *H influenzae* (including ampicillin-resistant strains), *Klebsiella* sp, *S aureus* (penicillinase- and non-penicillinase-producing), *S pyogenes*, and *E coli*.
2. **Urinary Tract Infections** caused by *E coli* and *Klebsiella* sp.
3. **Skin and Skin Structure Infections** caused by *S aureus* (penicillinase- and non-penicillinase-producing), *S pyogenes*, *E coli*, *Klebsiella* sp, and *Enterobacter* sp.
4. **Septicemia** caused by *S aureus* (penicillinase- and non-penicillinase-producing), *S pneumoniae*, *E coli*, *H influenzae* (including ampicillin-resistant strains), and *Klebsiella* sp.
5. **Meningitis** caused by *S pneumoniae*, *H influenzae* (including ampicillin-resistant strains), *N meningitidis*, and *S aureus* (penicillinase- and non-penicillinase-producing).
6. **Gonorrhea:** Uncomplicated and disseminated gonococcal infections due to *N gonorrhoeae* (penicillinase- and non-penicillinase-producing strains) in both males and females.
7. **Bone and Joint Infections** caused by *S aureus* (including penicillinase- and non-penicillinase-producing strains).

Clinical microbiological studies in skin and skin structure infections frequently reveal the growth of susceptible strains of both aerobic and anaerobic organisms. ZINACEF has been used successfully in these mixed infections in which several organisms have been isolated. Appropriate cultures and susceptibility studies should be performed to determine the susceptibility of the causative organisms to ZINACEF.

Therapy may be started while awaiting the results of these studies; however, once these results become available, the antibiotic treatment should be adjusted accordingly. In certain cases of confirmed or suspected gram-positive or gram-negative sepsis or in patients with other serious infections in which the causative organism has not been identified, ZINACEF may be used concomitantly with an aminoglycoside (see **PRECAUTIONS**). The recommended doses of both antibiotics may be given depending on the severity of the infection and the patient's condition.

Prevention: The preoperative prophylactic administration of ZINACEF may prevent the growth of susceptible disease-causing bacteria and thereby may reduce the incidence of certain postoperative infections in patients undergoing surgical procedures (eg, vaginal hysterectomy) that are classified as clean-contaminated or potentially contaminated procedures. Effective prophylactic use of antibiotics in surgery depends on the time of administration. ZINACEF® (sterile cefuroxime sodium, Glaxo) should usually be given one-half to one hour before the operation to allow sufficient time to achieve effective antibiotic concentrations in the wound tissues during the procedure. The dose should be repeated intraoperatively if the surgical procedure is lengthy.

Prophylactic administration is usually not required after the surgical procedure ends and should be stopped within 24 hours. In the majority of surgical procedures, continuing prophylactic administration of any antibiotic does not reduce the incidence of subsequent infections but will increase the possibility of adverse reactions and the development of bacterial resistance.

The perioperative use of ZINACEF has also been effective during open heart surgery for surgical patients in whom infections at the operative site would present a serious risk. For these patients it is recommended that ZINACEF therapy be continued for at least 48 hours after the surgical procedure ends. If an infection is present, specimens for culture should be obtained for the identification of the causative organism and appropriate antimicrobial therapy should be instituted.

CONTRAINDICATIONS: ZINACEF® is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

WARNINGS: BEFORE THERAPY WITH ZINACEF® IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEPHALOSPORINS, PENICILLINS, OR OTHER DRUGS. THIS PRODUCT SHOULD BE GIVEN CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS. ANTIBIOTICS SHOULD BE ADMINISTERED WITH CAUTION TO ANY PATIENT WHO HAS DEMONSTRATED SOME FORM OF ALLERGY, PARTICULARLY TO DRUGS. IF AN ALLERGIC REACTION TO ZINACEF OCCURS, DISCONTINUE THE DRUG. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE EPINEPHRINE AND OTHER EMERGENCY MEASURES.

Pseudomembranous colitis has been reported with the use of cephalosporins (and other broad-spectrum antibiotics); therefore, it is important to consider its diagnosis in patients who develop diarrhea in association with antibiotic use.

Treatment with broad-spectrum antibiotics alters normal flora of the colon and may permit overgrowth of clostridia. Studies indicate a toxin produced by *C difficile* is one primary cause of antibiotic-associated colitis. Cholestyramine and colestipol resins have been shown to bind the toxin in vitro.

Mild cases of colitis may respond to drug discontinuance alone. Moderate to severe cases should be managed with fluid, electrolyte, and protein supplementation as indicated.

When the colitis is not relieved by drug discontinuance or when it is severe, oral vancomycin is the treatment of choice for antibiotic-associated pseudomembranous colitis produced by *C difficile*. Other causes of colitis should also be considered.

PRECAUTIONS: Although ZINACEF® rarely produces alterations in kidney function, evaluation of renal status during therapy is recommended, especially in seriously ill patients receiving the maximum doses. Cephalosporins should be given with caution to patients receiving concurrent treatment with potent diuretics as these regimens are suspected of adversely affecting renal function.

The total daily dose of ZINACEF should be reduced in patients with transient or persistent renal insufficiency because high and prolonged serum antibiotic concentrations can occur in such individuals from usual doses.

As with other antibiotics, prolonged use of ZINACEF may result in overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

Nephrotoxicity has been reported following concomitant administration of aminoglycoside antibiotics and cephalosporins.

Interference with Laboratory Tests: A false-positive reaction for glucose in the urine may occur with copper reduction tests (Benedict's or Fehling's solution or with Clinitest® tablets), but not with enzyme-based tests for glycosuria (eg, Tes-Tape®). As a false-negative result may occur in the ferricyanide test, it is recommended that either the glucose oxidase or hexokinase method be used to determine blood plasma glucose levels in patients receiving ZINACEF.

Cefuroxime does not interfere with the assay of serum and urine creatinine by the alkaline picrate method.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Although no long-term studies in animals have been performed to evaluate carcinogenic potential, no mutagenic potential of cefuroxime was found in standard laboratory tests.

Reproductive studies revealed no impairment of fertility in animals.

Pregnancy: ***Teratogenic Effects: Pregnancy Category B:*** Reproduction studies have been performed in mice and rabbits at doses up to 60 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to cefuroxime. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: Since ZINACEF is excreted in human milk, caution should be exercised when ZINACEF is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in children below 3 months of age have not been established. Accumulation of other members of the cephalosporin class in newborn infants (with resulting prolongation of drug half-life) has been reported.

ADVERSE REACTIONS: ZINACEF® is generally well tolerated. The most common adverse effects have been local reactions following intravenous administration. Other adverse reactions have been encountered only rarely.

Local Reactions: Thrombophlebitis has occurred with intravenous administration in 1 in 60 patients.

Gastrointestinal: Gastrointestinal symptoms occurred in 1 in 150 patients and included diarrhea (1 in 220 patients) and nausea (1 in 440 patients). Symptoms of pseudomembranous colitis can appear during or after antibiotic treatment.

Hypersensitivity Reactions: Hypersensitivity reactions have been reported in less than 1% of the patients treated with ZINACEF and include rash (1 in 125). Pruritus, urticaria, and positive Coombs' test each occurred in less than 1 in 250 patients, and, as with other cephalosporins, rare cases of anaphylaxis, erythema multiforme, and Stevens-Johnson syndrome have occurred.

Blood: A decrease in hemoglobin and hematocrit has been observed in 1 in 10 patients and transient eosinophilia in 1 in 14 patients. Less common reactions seen were transient neutropenia (less than 1 in 100 patients) and leukopenia (1 in 750 patients). A similar pattern and incidence was seen with other cephalosporins used in controlled studies.

Hepatic: Transient rise in SGOT and SGPT (1 in 25 patients), alkaline phosphatase (1 in 50 patients), LDH (1 in 75 patients), and bilirubin (1 in 500 patients) levels has been noted.

Kidney: Elevations in serum creatinine and/or blood urea nitrogen and a decreased creatinine clearance have been observed, but their relationship to cefuroxime is unknown.

HOW SUPPLIED ZINACEF® is a dry, white to off-white powder supplied in vials and infusion packs.

Each vial contains cefuroxime sodium equivalent to 750 mg, 1.5 g, or 7.5 g of cefuroxime. ZINACEF in the dry state should be stored between 15° to 30° C (59° to 86° F), and protected from light.

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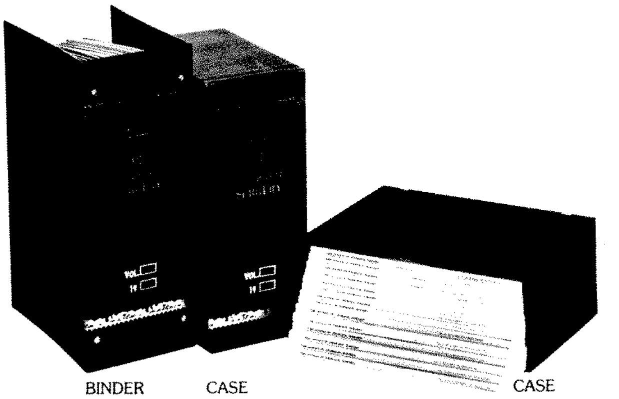

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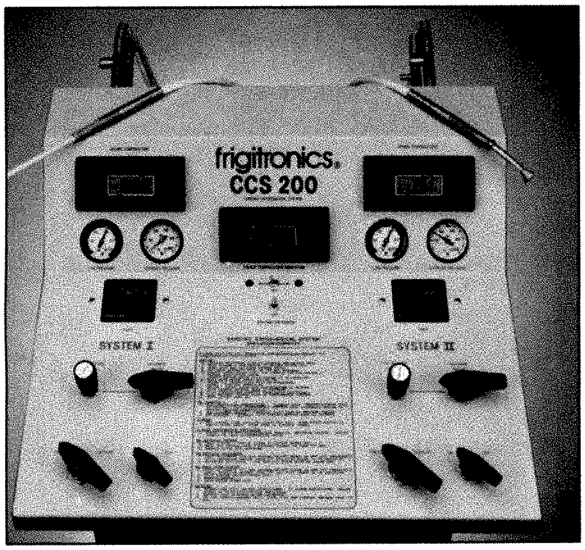

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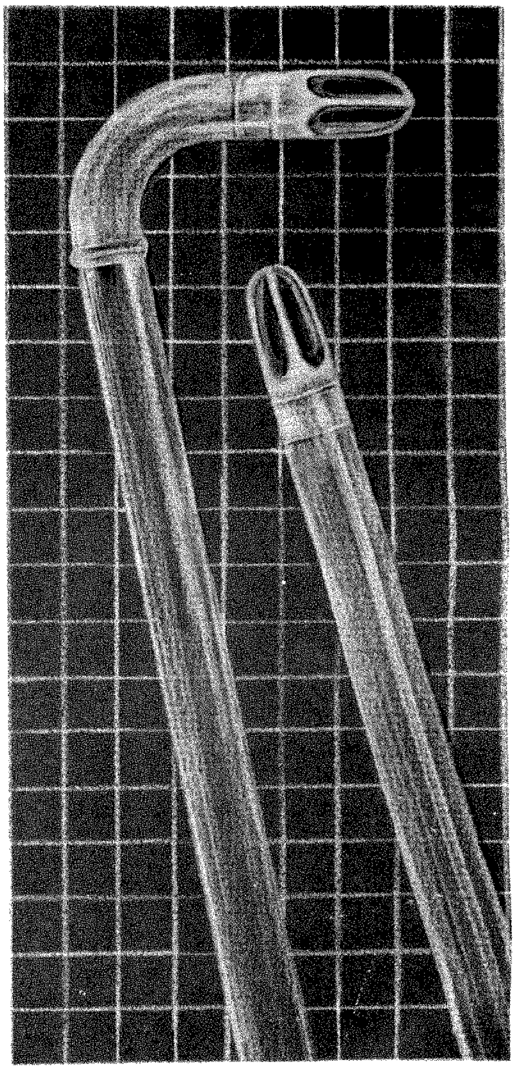

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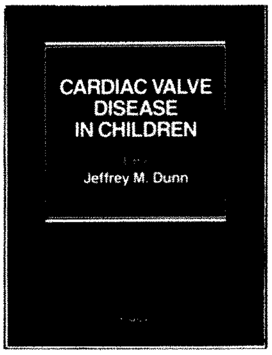

Edited by: **Jeffrey M. Dunn, MD**
Professor, Department of Surgery, Temple University School of Medicine; Director, Pediatric Heart Institute, Saint Christopher's Hospital for Children, Philadelphia, Pennsylvania

With 47 contributors

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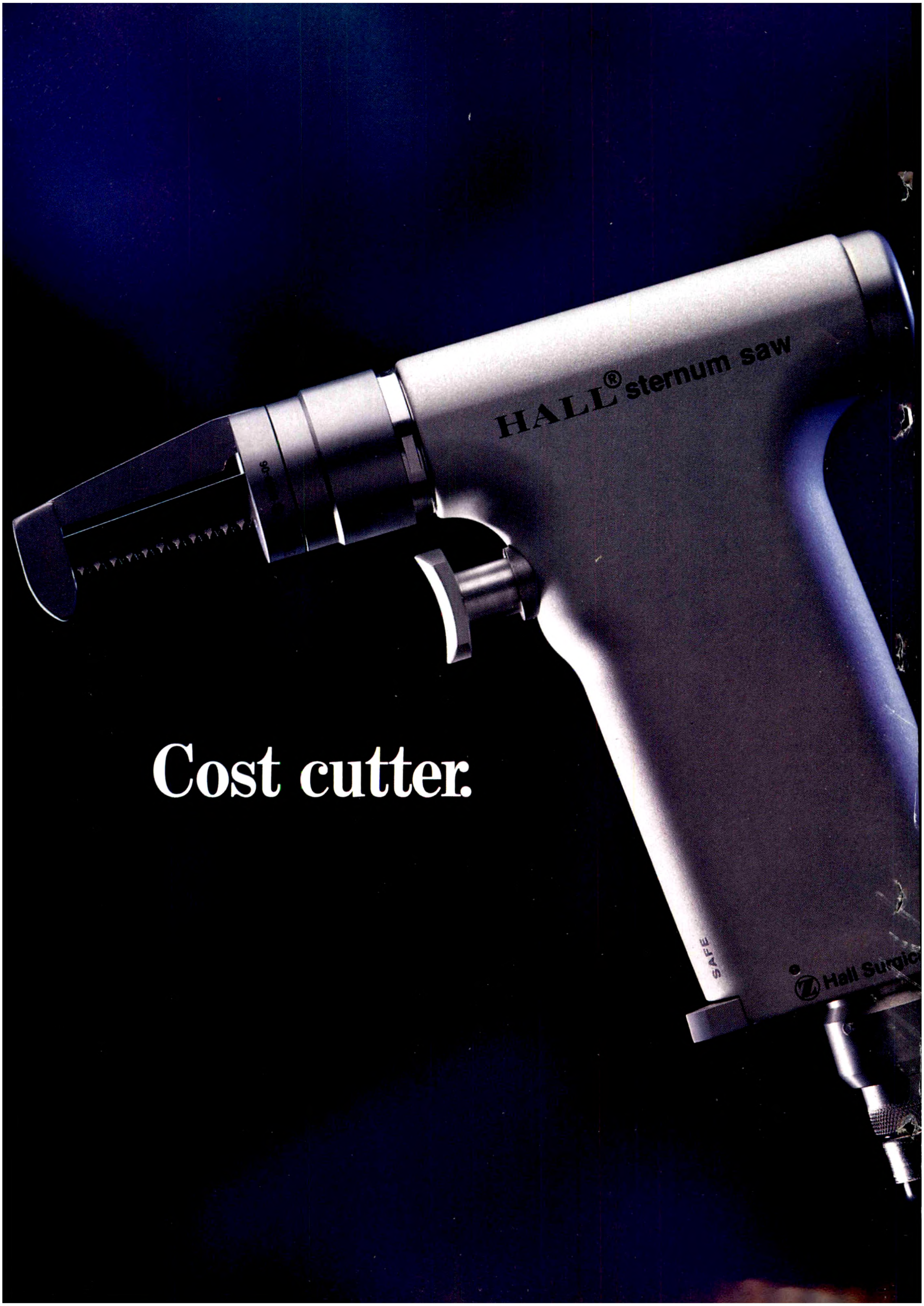
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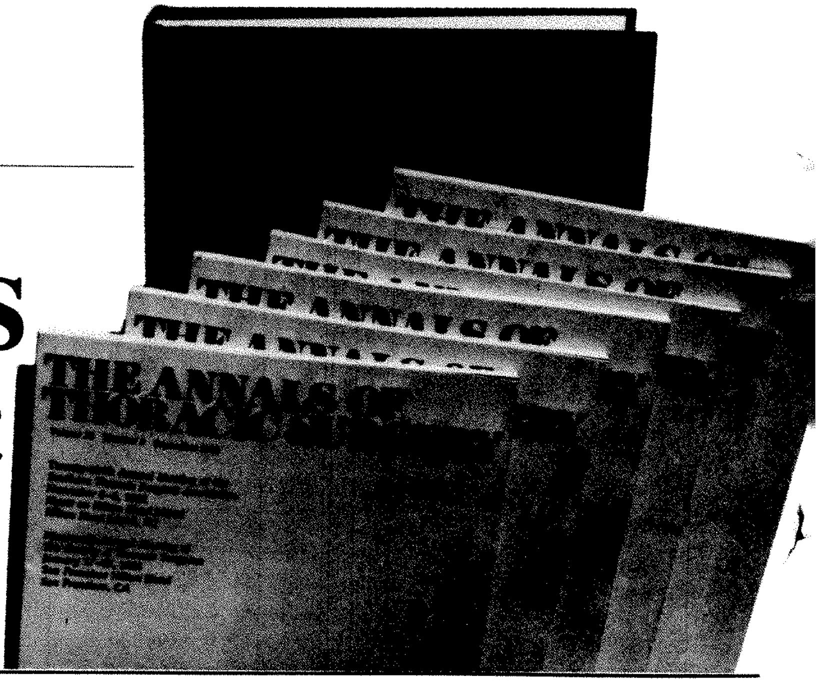

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Robert W. M. Frater, MD

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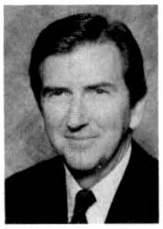
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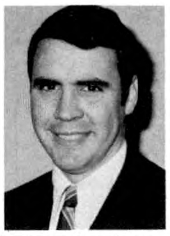
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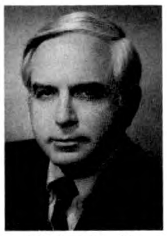
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Toward Fifty

Thomas B. Ferguson, MD

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On Volume 1, page 1 of *The Annals*, Paul C. Samson, first president of The Society of Thoracic Surgeons, in giving "La Raison d'Etre" for a new specialty surgical society and speaking for the original Council, concluded his remarks with this paragraph.

> We believe that The Society of Thoracic Surgeons has a well-defined place in the schema of surgical organizations. We believe that the Society is not competitive, but additive. We believe that the Society will attract gifted young practitioners of our specialty, and benefit from their contributions. We believe that the scope and opportunities of thoracic and cardiovascular surgery as a specialty will unquestionably be enhanced because The Society of Thoracic Surgeons exists.

Twenty-five years later, were he with us, Buck could take tremendous pleasure in how brief a time the beliefs of that little band of men have been realized. An international organization with 2,738 members, The Society exists in affirmation of a sound idea.

In this clement milieu *The Annals* has also flourished. Nurtured by its two parent organizations, and under the able stewardship of John D. Steele and Herbert Sloan, the journal earned its maturity stripes very early. Now our support derives from the thousands of cardiothoracic surgeons around the world who have "grown up" with *The Annals* during the past quarter century.

It is appropriate on a mountain climb to look back occasionally and see where you have been, and that is what we are doing in this issue, with commentaries by Bob Ellison, Society historian, and Herb Sloan, editor of *The Annals* during 15 of its 24 published years. We sit now on a comfortable perch, and the pathway statistics are impressive. We record an increase in subscribers every year since the beginning. The number of manuscripts processed has increased every year to more than 900 at present; this figure represents a threefold increase since 1969. The editorial board has been enlarged from 14 original members to 21 in 1969 to a current 26 members. In 1966, we had 15 guest reviewers, last year we needed 208. *The Annals* has been profitable for The Society of Thoracic Surgeons each year since 1969.

These numbers, however, do not tell the important story, that of quality. This standard was set by John Steele at the outset, and our proudest accomplishment is the unwavering maintenance of that standard. For this *The Annals* is indebted to the guest reviewers who willingly give their time, and to the members of the editorial board, past and present, who do the work, set the tone, and shape the direction of this journal—all of these men and women have the heartfelt thanks of three editors, every Society member, and every subscriber. And of the staff personnel, two deserve special mention for their contributions in so many ways: Jeanne Tashian Fitzgerald, administrative editor for many years, and Carol L. Blasberg, who has held this position since 1984.

Little, Brown and Company has published *The Annals* since the beginning. Journal publishing is a business, done by contract agreement, but the editorial office of every journal develops a rapport with its publisher born of the necessary daily communication. The relationship between *The Annals* and Little, Brown was special beyond this; they shared the experience of entering into a new venture and having that venture succeed. Including Fred Belliveau, who seemed more like one of our own than one of theirs, our quarter century of cordial memories includes a now large list of managing editors, copy editors, artists, and others, all dedicated to the quality of *The Annals*.

But reflections on the past should by nature be brief, as they are in this issue, because, to paraphrase Satchel Paige, you can't look ahead if you're looking back. And looking ahead has captured the attention of the editorial office, the Annals Liaison Committee, and The Society Council for a large part of the past 2 years. The result you hold now: we have a new publisher, a new format, and many other changes that will become apparent in time. Are we changing publishers for a "new look"? Nothing could be further from the truth. All publishers will respond to a request for a new shade of makeup. The decision was based on our perception, studied very thoroughly, that Elsevier Science Publishers, one of the largest journal publishers in the world, is best suited to meet the needs of *The Annals* as we enter our second quarter century of service to the cardiothoracic surgery community. Many of our plans go beyond the printed page into all aspects of electronic communication. We think it is an exciting time. This first issue of our 25th anniversary year carries a message from our current president, George G. Lindesmith, and the Herbert Sloan Lecture, as well as papers from the Circulatory Support Symposium held in February 1988.

You, the reader, have the assurance of The Society, the editorial board, the editorial office, and Elsevier Science Publishing Company that we will persist in our efforts to make *The Annals* an even better, more responsive publication than in the past. We seek your suggestions for constructive change, and guarantee that all ideas will receive serious consideration. The philosophy of *The Annals* continues to be as stated by John Steele in the first issue: "your comments, criticisms, and contributions as readers are invited—so that *The Annals* may consistently and successfully combine authoritativeness with vitality," and by Herb Sloan, whose words are carried on the title page of every issue, "to provide a place for *all* thoracic surgeons to relate experiences which will help other practicing thoracic surgeons give better patient care."

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The Early Years

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The Society of Thoracic Surgeons

The history of the origin and development of The Society of Thoracic Surgeons has been presented in some detail on three previous occasions [1–3]. In the late 1950s and the early 1960s thoracic and cardiac surgery rapidly expanded into an identifiable specialty. An increasing number of thoracic surgeons were being trained without an organization with which they could be identified, as The American Association for Thoracic Surgery did not wish to enlarge its membership. For several years the possibility of a new organization was discussed in great detail at the annual meetings of the John Alexander Society, and the final impetus for formation of a new society came from a report to this Society by a special committee composed of Drs Francis X. Byron, J. Maxwell Chamberlain, R. Adams Cowley (Chairman), Byron H. Evans, Earle B. Kay, Edgar P. Mannix, John E. Miller, John D. Steele, and Clifford F. Storey [4].

Dr Steele (Fig 1), well recognized for his editorial skills, was editor of the John Alexander Monograph Series, a series of monographs contributed to by Dr Alexander's former trainees and published in Dr Alexander's honor. He felt quite strongly that the success of the new Society would depend upon a new journal that would be the spokesman for the organization. It was not unexpected, therefore, that Dr Steele was selected to be editor of the new journal at a meeting of the founding members held at the Fairmont Hotel in San Francisco on October 31, 1963, during the Clinical Congress of the American College of Surgeons.

Dr Steele had obviously given considerable thought to and done background planning for the establishment of this new journal. At the first Executive Committee and Council Meeting in St. Louis on December 20, 1963, his report included the naming of the journal to be "The Annals of Thoracic Surgery," and he presented a list of associate editors and editorial board members to be approved by the Council. In addition, he reported the results of his efforts to obtain a publisher for the new journal [5]. Somewhat to his surprise and dismay, two publishing houses had rejected his proposal completely, and a third demanded a $45,000 advance escrow fund for use against potential losses. At that time the Medical Book Division of Little, Brown and Company of Boston did not publish a medical journal, and for this reason Dr Steele had not contacted them. Dr Ralph D. Alley, one of the early advocates of the new Society and a member of the Council, suggested that Little, Brown be approached, and Dr John Strieder of Boston, also a member of the original Council, was assigned to be The Society's emissary. Just before departure from the St. Louis airport Dr Alley telephoned Mr Fred Belliveau (Fig 2), a vice-president of Little, Brown and general manager of its Medical Book Division, to apprise him of the desire of The Society to establish a journal (Alley RD, personal communication, July 1988). Dr Alley assured him that the new organization was going to be a success [2]. Unquestionably, Dr Alley's prior acquaintance with Mr Belliveau strengthened the ensuing negotiations that resulted in the 25-year relationship between The Society of Thoracic Surgeons and Little, Brown and Company.

Within the historical files of The Society there are numerous letters of correspondence between Dr Strieder, Dr Steele, and Mr Belliveau relating to the establishment of *The Annals*. Correspondence to Dr Steele describes a luncheon meeting between Dr Strieder and Mr Belliveau that set the stage for further talks between editor and publisher. This luncheon probably was held in one of the small, quaint restaurants in the vicinity of No. 34 Beacon Street, office of Little, Brown and Company. Such restaurants were frequented by literary personnel living in the area.

As a result of negotiations between these two men, a 5-year contract was signed on March 30, 1964, for publication of a bimonthly journal consisting of 96 pages in each issue. Initially, Mr Belliveau felt that it would be at least a year before the first issue could be published. However, it had been Dr Steele's dream to have the first issue ready at the time of the first annual meeting of The Society in St. Louis in January 1965. In spite of Mr Belliveau's objections and as a result of Dr Steele's perseverance, the first issue of *The Annals* was indeed available at the first meeting (Fig 3).

At the original Council meeting in St. Louis on December 20, 1963, one agenda item concerned a proposal to negotiate with the Southern Thoracic Surgical Association to publish some of the papers presented at their annual meetings [5]. This proposal was favorably received by the Southern Thoracic Surgical Association as a number of members were also active in the founding and development of The Society of Thoracic Surgeons. Accordingly, on October 5, 1964, the Council of The Society approved *The Annals of Thoracic Surgery* to be the official journal of The Society of Thoracic Surgeons and the Southern Thoracic Surgical Association. This relationship was also approved by the Southern Thoracic Surgical Association at its Council meeting in November 1964. Beginning in January 1971, the title page has depicted the seals of the two organizations.

As a result of Dr Steele's unusual editorial talents,

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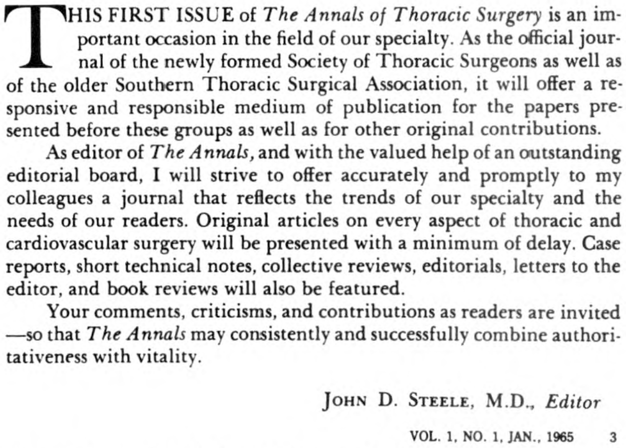
Fig 1. John D. Steele, MD, founding editor of The Annals of Thoracic Surgery *(1963–1969).*

supported by two very effective associate editors, Dr David J. Dugan of Oakland, California, and Dr Herbert Sloan of Ann Arbor, Michigan, and with a diligent editorial board, *The Annals of Thoracic Surgery* flourished.

Fig 2. Fred Belliveau, vice-president of Little, Brown and Company and general manager of its Medical Book Division.



THIS FIRST ISSUE of *The Annals of Thoracic Surgery* is an important occasion in the field of our specialty. As the official journal of the newly formed Society of Thoracic Surgeons as well as of the older Southern Thoracic Surgical Association, it will offer a responsive and responsible medium of publication for the papers presented before these groups as well as for other original contributions.

As editor of *The Annals*, and with the valued help of an outstanding editorial board, I will strive to offer accurately and promptly to my colleagues a journal that reflects the trends of our specialty and the needs of our readers. Original articles on every aspect of thoracic and cardiovascular surgery will be presented with a minimum of delay. Case reports, short technical notes, collective reviews, editorials, letters to the editor, and book reviews will also be featured.

Your comments, criticisms, and contributions as readers are invited —so that *The Annals* may consistently and successfully combine authoritativeness with vitality.

JOHN D. STEELE, M.D., *Editor*

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Fig 3. Comments of Editor Steele in the first issue of The Annals.

In the early days, Dr Steele was concerned about the volume of quality papers suitable for publication in *The Annals*, but time proved his fears unwarranted. At the Council meeting on January 23, 1966, he reported that during the prior year it was necessary to exceed the 96 contract pages for a total cost of $4,635 for extra pages [6]. For this reason, the Council approved publication of *The Annals* on a monthly basis beginning with the January 1967 issue. Since that time *The Annals* has had an increase in the number of pages annually.

As The Society prospered and the membership increased, exceeding 800 by the January 1969 meeting, *The Annals* prospered with a circulation approximating 3,000 by that time. Regrettably, because of illness, Dr Steele resigned as editor effective at the time of that annual meeting and was succeeded by Dr Herbert Sloan of Ann Arbor, Michigan. At the meeting Dr Steele received an ovation for his outstanding contributions to The Society as founding editor of *The Annals of Thoracic Surgery*. He was presented with the first Distinguished Service Award by The Society in recognition of these accomplishments.

Dr Steele undoubtedly advanced the purposes of The Society of Thoracic Surgeons by his editorial skills and his determination to produce a high quality journal in a relatively short period.

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More Change

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Twenty-five years! It seems incredible that so much time has passed since the initial issue of *The Annals of Thoracic Surgery* was distributed at the first annual meeting of The Society of Thoracic Surgeons in January 1965. Yet, the story really began several years earlier when increasingly active discussion of the need for a new thoracic surgical society started. Our founders envisioned an organization that would provide a forum for all qualified thoracic surgeons.

Most believed strongly that the new Society needed a vigorous and successful journal in order to succeed. John Steele was chosen as editor at the founding members meeting of The Society of Thoracic Surgeons in October 1963. He had had extensive experience as editor of the John Alexander Monograph Series and was the obvious choice to head the new journal.

The tortuous path followed to find a publisher, which was ultimately Little, Brown and Company of Boston, is reviewed by Bob Ellison on pages 4–5 of this issue. As noted, the path included a now famous lunch where John Strieder, a Bostonian and member of the original Council of The Society of Thoracic Surgeons, sounded out Fred Belliveau, head of the Medical Books Division of Little, Brown. Fred says he was able to negotiate a several martini lunch successfully and thus gain the approval of Dr Strieder. The first contract with Little, Brown followed shortly thereafter.

At this stage in the organization and development of the new society, Tom Burford, Max Chamberlain, and Buck (Paul) Samson emerged as the strongest leaders. Their backgrounds included training by Evarts Graham or John Alexander. Most of the members of the new editorial board also had been trained in either St. Louis or Ann Arbor or had a personal relationship with The Society's leaders.

John Steele and others of us on the editorial board believed it was of the utmost importance to have the first issue of the journal available at the first annual meeting of The Society of Thoracic Surgeons. There was genuine concern as to whether or not the new Society would survive, and having a journal in place would help tremendously. By dint of extraordinary effort on the part of John and his editorial board, Volume 1, Number 1 of *The Annals of Thoracic Surgery* was distributed at that meeting in January 1965.

The journal had a quality of excellence from the beginning. For example, the editor and the editorial board insisted that all Society papers be reviewed to assure they met *The Annals'* standards rather than be accepted routinely simply by virtue of the fact that they were presented at the annual meeting. It is interesting that a welcome to the new Society and its journal appeared as an editorial in the *New England Journal of Medicine* [1].

In the first issue of *The Annals*, Buck Samson, The Society's first president, reviewed the need for a new thoracic society. John Steele outlined succinctly the goals of the new journal, and the first issue contained many of the elements he wished to see included. It provided information for the practicing thoracic surgeon that would help in the care of patients. It covered the entire field of thoracic and cardiovascular surgery, and it provided a forum for practicing thoracic surgeons.

There were to be six issues a year of 96 pages each. Within 2 years it was necessary to make *The Annals* a monthly. Early on the need to publish extra pages to accommodate the material available become apparent and this was to be a continuing problem for years.

John almost singlehandedly pulled each issue of the journal together, and there were a good many problems resolving differences between the editor and Little, Brown, itself new to medical journal publishing. The editorial board provided excellent support in reviewing manuscripts, but John encountered another problem that never quite disappeared, that of getting manuscripts returned on a timely basis from reviewers. (Somewhat later a prize was given to the most prompt reviewer. Tom Ferguson won it routinely. We never quite dared to give one to the slowest reviewer, although we had some strong candidates.)

In early 1969 John realized he could no longer continue as editor because of illness, and he arranged for an orderly transfer of responsibility to my office in Ann Arbor. In recognition of his outstanding contributions, he received the first Distinguished Service Award of The Society. John accepted the award with the grace and courage he had always shown. It is unlikely that any other person in thoracic surgery could have accomplished what he did in bringing *The Annals* through its formative period. He continued to review manuscripts and offer help until he died in his sleep on July 27, 1969.

The new editor had to relearn many of the lessons John Steele knew so well. He quickly discovered that reviewers are a chancey lot. Two reviewers of equal stature, each well respected in the field, often returned diametrically opposed evaluations of the same manuscript. The editor frequently found himself adjudicating these differences of opinion. Review promptness became a Holy Grail.

An editorial assistant was hired. The University of Michigan provided space and support for the editorial office. The organization of the manuscript flow was time-consuming, and efforts were made to encourage the early

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submission of manuscripts to the journal before presentation at the annual Society meetings. Relations with Little, Brown needed to be cemented and several trips to Boston were made by the editor and his assistant.

Nancy Megley at Little, Brown became managing editor of *The Annals* in 1969. Within a few years Jeanne Tashian Fitzgerald became the administrative editor in Ann Arbor. Both of them made major contributions to the success of *The Annals*. With the continuing support and interest of Fred Belliveau and Nancy's skillful management, most production problems of *The Annals* were solved.

Efforts could now be directed toward meeting new, more ambitious goals. Particular attention was paid to manuscripts, often of foreign origin, that had valuable data to present but were not well written. If a manuscript contained important material, the editorial office made every effort to revise it into an acceptable form. Younger authors were encouraged to submit manuscripts to *The Annals*. Great care was taken with illustrations because they contributed so much to the overall appearance of the journal.

I suppose it can be said that we saw ourselves as the "Avis" of thoracic surgery journals, so we tried harder. The long and distinguished history of the "gray journal," whose circulation figures always seemed to be an elusive 2,000 subscribers above ours, spurred us to be more creative and to continually seek ways to make ourselves better.

Abstracts were placed at the beginning of each article. Editorials were solicited as comments on original articles in the same issue and were placed at the front of the journal. The How to Do It, Classics in Thoracic Surgery, and Thoracic Surgery Quiz sections were introduced. Reproduction of color photographs became available for authors. A classified advertising section was started to provide a place to look for a job or a partner.

Efforts were made to standardize nomenclature and methods of reporting data. Biostatistical analysis of manuscripts was introduced through an agreement with the Department of Biostatistics at the University of Michigan School of Public Health.

As *The Annals* became more widely recognized, in a few years the backlog of manuscripts to be published grew from three or four articles to three or four issues, despite an increasing rejection rate.

A plan for regular rotation of editorial board members was instituted to allow new faces on the board. In the late 1970s, in recognition of the strong relationship that existed between US and Canadian thoracic surgeons, we added two distinguished men from Canada to the board: Tony Dobell from Montreal and Frank Tyers from Vancouver.

In 1976 an entirely new format for *The Annals* was created under the supervision of Clif Gaskill, then production manager in Little, Brown's Medical Division. This larger, two column layout with smaller type allowed more material to be printed per page, but the change was in part a response to advertisers who were imposing size criteria on all medical journals and who, increasingly, found *The Annals* a desirable journal in which to advertise. Originally, the title of the journal was placed at the bottom of the cover. When a medical librarian's research showed that the title could not be read on most library shelves, the title was shifted to the top. The original chartreuse color of the cover was attention-getting but was something of an afterthought, without any specific relation to The Society or its specialty.

In 1982, under mandate from its editorial board, *The Annals* joined the computer revolution and purchased an IBM personal computer to help manage the increasing numbers of manuscripts that came into and went out of the editorial office every day. Continuing refinement of the programs and newer, more sophisticated equipment made the management of *The Annals'* data base easier, more useful, and more accurate.

The Annals began to turn over a profit to Little, Brown in 1969 and has made money almost every year since that time. In 1969 there were 2,784 subscribers; today *The Annals* can claim 8,050 subscribers. It has gained acceptance as one of the important journals in the field, and the number of manuscripts handled has tripled since 1969.

The members of the editorial board, present and past, deserve the highest praise for their contributions and their dedication to the goal of publishing the best journal possible. Each should be thanked publicly, particularly those who served as associate and assistant editors. Without the members of the editorial board *The Annals* would not be.

Especially, I would like to cite those who took on duties above and beyond the never-ending job of manuscript review: Tim Takaro, associate editor in charge of soliciting editorials; Dick Hughes, associate editor, who arranged for submission of collective reviews; Marvin Kirsh, associate editor, who created and oversaw the Classics in Thoracic Surgery; Dick Peters, assistant editor and book review editor; and Hassan Najafi, assistant editor, who created and managed the Thoracic Surgery Quiz.

Now *The Annals* is changing again, and change is important if *The Annals* is to maintain its place [2]. Tom Ferguson became editor in 1984 and is carrying out his own plans to keep *The Annals* in the forefront of thoracic surgery. This now means a new publisher and another change in format, as he places his own stamp on the journal. He goes forward with the firm support of all of us who have had the privilege of contributing to *The Annals* in the past.

Thanks are owed to all the members of the original editorial board who shared their memories of those early times with me. I appreciate particularly the long letters from Fred Belliveau and Nancy Megley, as well as the recollections of that fabulous raconteur, Ralph Alley. Jeanne Tashian Fitzgerald also shared her memories with me and provided invaluable editorial help.

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Looking Ahead

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If we consider the time for planning and organization prior to publication of the first issue of *The Annals of Thoracic Surgery* in January 1965, with this issue it has reached its 25th birthday, paralleling the development of The Society of Thoracic Surgeons. In this time span, *The Annals* has arrived at a stage of maturity comparable with *The Journal of Thoracic and Cardiovascular Surgery,* which has now had 58 years of growth and experience from the time of its first publication in 1931. *The Annals,* as well as The Society of Thoracic Surgeons, has maintained a focus on the clinical aspects of all areas of thoracic and cardiovascular surgery. By virtue of this posture, *The Annals* has become, and remains, a primary educational tool for those practicing our specialty.

The relationship between The Society and *The Annals* has been crucial to the development of both. The Society instigated and supported the production of our journal to serve as The Society's "window to the world." Under the direction of its editors, *The Annals* has fulfilled this function in an outstanding way.

The future of the publication seems secure. The close relationship to The Society must be jealously guarded and maintained. Under the stewardship of the current editor, Dr Ferguson, and his successors, we can anticipate continued growth, not only in distribution but in those exciting new areas of communication technology that are becoming available. Continuing efforts to expedite the dissemination of the printed word I see as being productive, but also innovative ventures into audio and visual presentation of scientific data may well become an important role for *The Annals*, its editor, the staff, and The Society. The rapidly advancing communication technology would support this as a logical step for The Society and its journal.

Over the past several years, *The Annals* has been used by The Society as a medium to present to its members, as well as to the profession at large, The Society's stance on various medical and nonmedical issues that are points of controversy. In today's changing world, I see *The Annals* being used even more in this manner, wherein postures of The Society, its council, and its committees will be officially recorded and presented not only to thoracic surgeons but to the medical profession in general. I believe this use of *The Annals* by The Society will become increasingly important, particularly over the next few years.

I envision the next quarter century of *The Annals of Thoracic Surgery* as being prosperous, successful years of exciting, continuing growth.

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Notes on the Windpipe

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A bas relief on the facade of the Cathedral at Orvieto depicts the birth of Eve (Fig 1). God, very much the thoracic surgeon, works through a respectable thoracotomy. Dr Edward D. Churchill first brought this interpretation to my attention, although his photograph of it was uncluttered by plastic shields now made necessary by the new barbarians. Although this may well have been the first thoracic surgical procedure, we generally recognize our specialty as a relatively new one. After the employment of Sauerbruch's negative pressure chamber and various positive pressure devices such as those of Brauer and Robinson [1, 2], endotracheal intubation finally allowed the thoracic surgeon to get in and out of the chest with a surviving patient. Dr Churchill once laughingly called his pioneering generation "buccaneer surgeons." They were able to slash their way into the chest, thanks to the endotracheal tube, and in it they found the treasures of pulmonary, esophageal, and mediastinal pathology. These prizes of a previously inaccessible area of surgery lay before them to be grasped. About 25 years later another gadget—the heart-lung machine—permitted a second wave of buccaneers to plunge into the heart. Once again much good was done and great reputations were made.

Although tracheostomy is one of the most ancient of operations, the windpipe was all but ignored during this early surge into the chest. Ambroise Paré sutured two severed cervical tracheas in the 16th century [3], unfortunately without survival, but in the first burst of modern thoracic surgery, little was done with the trachea. There were some reports of resections with end-to-end anastomosis, usually for short lesions, and numerous lateral excisions with patching of the tracheal defect. Early recurrence of tumor was the rule. In the laboratory and less often in the operating room, attempts were made to replace the trachea with a variety of prosthetic materials, alone or combined with native tissues [4].

Why was this the case? Why so little progress? First, there were anatomical difficulties in reconstruction. It was believed to be impossible to resuture predictably the trachea if more than 2 cm were resected [5]. It was also believed that cartilage healed poorly. Second, it seemed difficult to maintain anesthesia and oxygenation during extensive surgical procedures on the trachea. And last, but perhaps most important, few tracheal lesions were seen. Primary tumors of the trachea were rare then as now, and operation was not considered for secondary neoplasms. Benign strictures were also rare. The challenge was therefore limited.

In the last 25 years, the following changes have occurred in tracheal surgery.

1. All but the most extensive lesions are now surgically removable.
2. The techniques of tracheal surgery and anesthesia have been developed and standardized to a considerable degree.
3. The pathology of tracheal diseases, both neoplastic and inflammatory, is much better understood and therefore more amenable to appropriate treatment.

These changes resulted from the efforts of numerous surgeons in a number of countries. I shall relate to you a rather personal account of this last buccaneering sally of thoracic surgery—the attack on the trachea over the last 25 years. I describe this as a personal account because I have no intention of slighting the many contributors whom I shall not mention in this brief and anecdotal account. It is not a review of the development of tracheal surgery. I also wish to present this account as an extended exercise in experimental surgery. In it are intertwined the threads of laboratory investigation and clinical research, with the story moving back and forth from laboratory to operating room as problems arise. There are some lessons to be learned from this experience. I hope the story will be of interest, especially to young surgeons embarking on careers in thoracic surgery. For the rest of you who might now be groaning silently, "There he goes, talking about the windpipe again," I can only point out that I am simply recognizing that this subject is why I'm standing before you here today.

The Ether Dome of the Massachusetts General Hospital is the hospital's original operating room atop the Bulfinch Building (Fig 2). Here is where general anesthesia for surgery was first publicly demonstrated to the medical community and from where it spread throughout the western world. I was seated in a back row of the Ether Dome, now a teaching amphitheater, one Tuesday morning in 1961 at the medical-surgical pulmonary conference when a patient with a cylindroma in the lower trachea was presented. The lesion was extensive, and lateral resection with appropriate patching was proposed. Dr Churchill commented on the problems of leakage of such patches, a not infrequent occurrence, with resultant mediastinitis and usually death when such occurred in the thorax. This, he pointed out, was quite in contrast to the neck, where the patient could live to fight another day while secondary repairs were tediously completed. It occurred to me that in severe blunt trauma to the neck with tracheal separation, the surgeon usually found that

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Fig 1. The first thoracic surgical procedure. The birth of Eve, from the facade of the Duomo at Orvieto, Italy.

the distal trachea had slipped into the thorax. I suggested that we might consider electively dropping a segment of trachea into the chest to accomplish safe intrathoracic reconstruction and complete the cervical reconstruction later. Dr Churchill accepted this with his usual tolerance for the ideas of the young, but I cannot remember that it generated much enthusiasm from anyone present.

The idea persisted. After a time it seemed to me to be worth investigating. Given the erratic and generally disastrous results of prosthetic replacement of the trachea, I decided that any reconstruction I might attempt would be based on use of the patient's own tissues. The initial questions were as follows. First, how much trachea could one resect and still bring the ends together primarily? Second, if one really did devolve the cervical trachea into the chest, what would be the best way to reconstruct the cervical trachea?

At that time I was working in the laboratory with Dr Jerome Gross (Fig 3), in an effort to apply some of his vast knowledge of collagen and connective tissue to problems

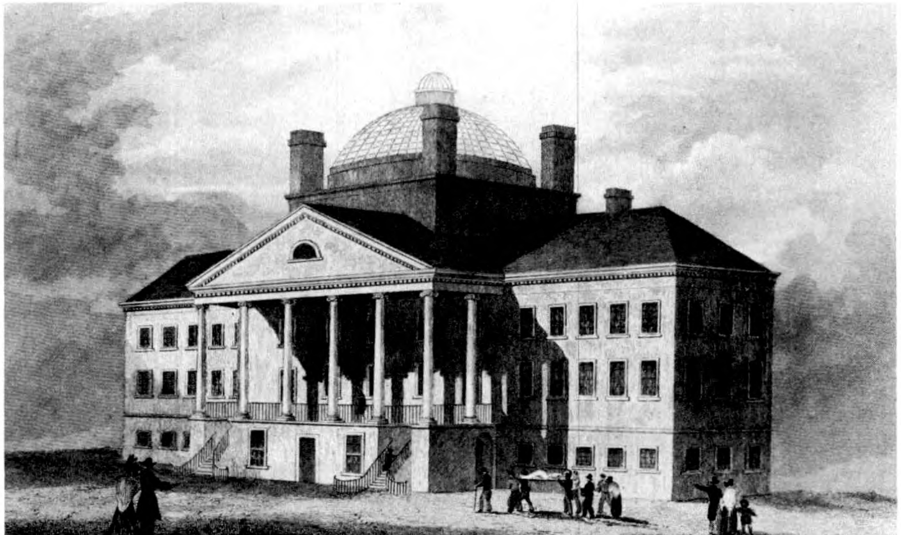

Fig 2. The Bulfinch Building, Massachusetts General Hospital, in 1823. The Fenner-Sears print. The operating room was located under the dome. The first operation performed was on September 21, 1821. Here was made the first public demonstration of general anesthesia for surgery on October 16, 1846. The "Ether Dome" is now a conference room.

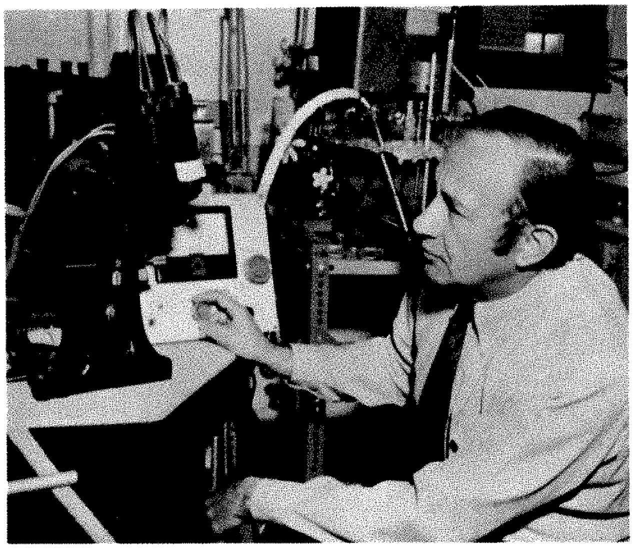

Fig 3. Dr Jerome Gross, Chief of the Lovett Laboratories, Department of Medicine, Massachusetts General Hospital. He taught and stimulated many young physicians and scientists who went on in research and clinical careers, enriched by their experience and contact with his innovative mind.

of wound repair. I mention this because I am convinced that these studies were important to me methodologically in subsequent work on the trachea. From work on the biology of wound contraction and wound collagenases, I believe I learned something about experimental methods [6, 7]. From additional work with reconstituted collagen for use as a surgical prosthetic material, I learned what one can expect from implantation of biological materials [8]. A most important lesson was that one cannot repeal the laws of wound repair. The young surgical investigator who proposes to design new operations will do well to ground himself in a thorough knowledge of tissue responses to injury and the processes of repair.

As young surgeons in those days were not deluged with patients as they seem to be today, I did find time to embark on both tracheal projects almost simultaneously. The first was to investigate in the dissecting room the potential for reapproximation of the human trachea after excision of various lengths of thoracic trachea, measuring the tensions necessary to approximate the ends and working out methods of mobilization that might ease anastomotic tension. At the same time in the experimental laboratory, we worked on methods to reconstruct the cervical trachea to close the gap that I presumed would occur when a segment of cervical trachea was devolved with its blood supply into the mediastinum. I was assisted in these efforts by two devoted young surgeons, Dr Ellen Dignan and Dr Tsuyoshi Miura from the University of Tokyo. For cervical tracheal replacement we eventually settled upon a multistaged method, using a bipedicled flap of skin and underlying platysma that was splinted with polypropylene rings inserted between the dermis and platysma [9] (Fig 4).

Mobilization studies indicated that approximately one half of the human adult trachea could be removed and the ends brought together in a predictable fashion without excessive tension [10] (Fig 5). I failed then, as so many young investigators do, to explore the literature thoroughly before embarking on the project. However, I was reassured to find later that Michelson and colleagues had arrived at similar conclusions in 1961 [11].

A question still remained. How could anesthesia and ventilation be maintained? I had early put aside cardiopulmonary bypass, believing that the anticoagulation was unwise in intrathoracic resection, in which the lung might well have to undergo substantial manipulation. This was even more the case in patients who might have limited pulmonary function. I turned for a solution of this problem to an imaginative anesthetist, Dr Henrik Bendixen, who was one of a group of anesthesiologists at Massachusetts General Hospital who developed one of the very first respiratory intensive care units in the United States. We had numerous blackboard sessions in which we worked out techniques that we would use for direct intubation across the operative field using flexible armored tubing. The guiding principle was to work out a method by which the patient would be continuously under complete ventilatory control and remain fully oxygenated, so that there would be no periods of hurry or crisis during reconstruction.

Just as we concluded these initial experiments and preparations, Dr Earle Wilkins identified a tracheal tumor as the cause of a 48-year-old woman's slowly progressive dyspnea over 5 years. She could now only breathe stridorously sitting up, leaning forward. After bronchoscopy, which demonstrated a highly obstructive lesion in what I thought was the lower trachea, obstruction worsened that evening (November 26, 1962) and the patient was hustled to the operating room. The approach was a right cervico-mediastino-thoracic trapdoor incision that would give access to the entire trachea if there was need. I was startled to find that this was not a tumor of the lower trachea at all, but a carinal "cylindroma." My thinking at that point had not yet progressed to the knotty problem of carinal reconstruction. After resection of the tumor, I looked at the three open ends of trachea and bronchi and wondered what to do next. Dr Bendixen mercifully broke the tension as he looked into the wound from the head of the table, commenting as the patient breathed in and out of the left main bronchus, "Well, that certainly does cut down on the dead space." However, on the basis of work already done, it was possible to perform reconstruction, suturing the right main bronchus end-to-end to the trachea and the left bronchus end-to-side [12] (Fig 6). My assistant was the chief resident, Harold Urschel. I am happy to say that the patient did indeed survive and lived more than 17 years before returning with recurrent carcinoma. Two further lessons about adenoid cystic carcinoma of the trachea were learned then: one was the need for follow-up for greater than 10 years, and the other was that postoperative irradiation is probably advisable even where margins and lymph nodes are negative.

I probably would have examined the question of carinal reconstruction in the autopsy room and experimental laboratory had I not been propelled by this first case into an unplanned operating room experiment. With its suc-

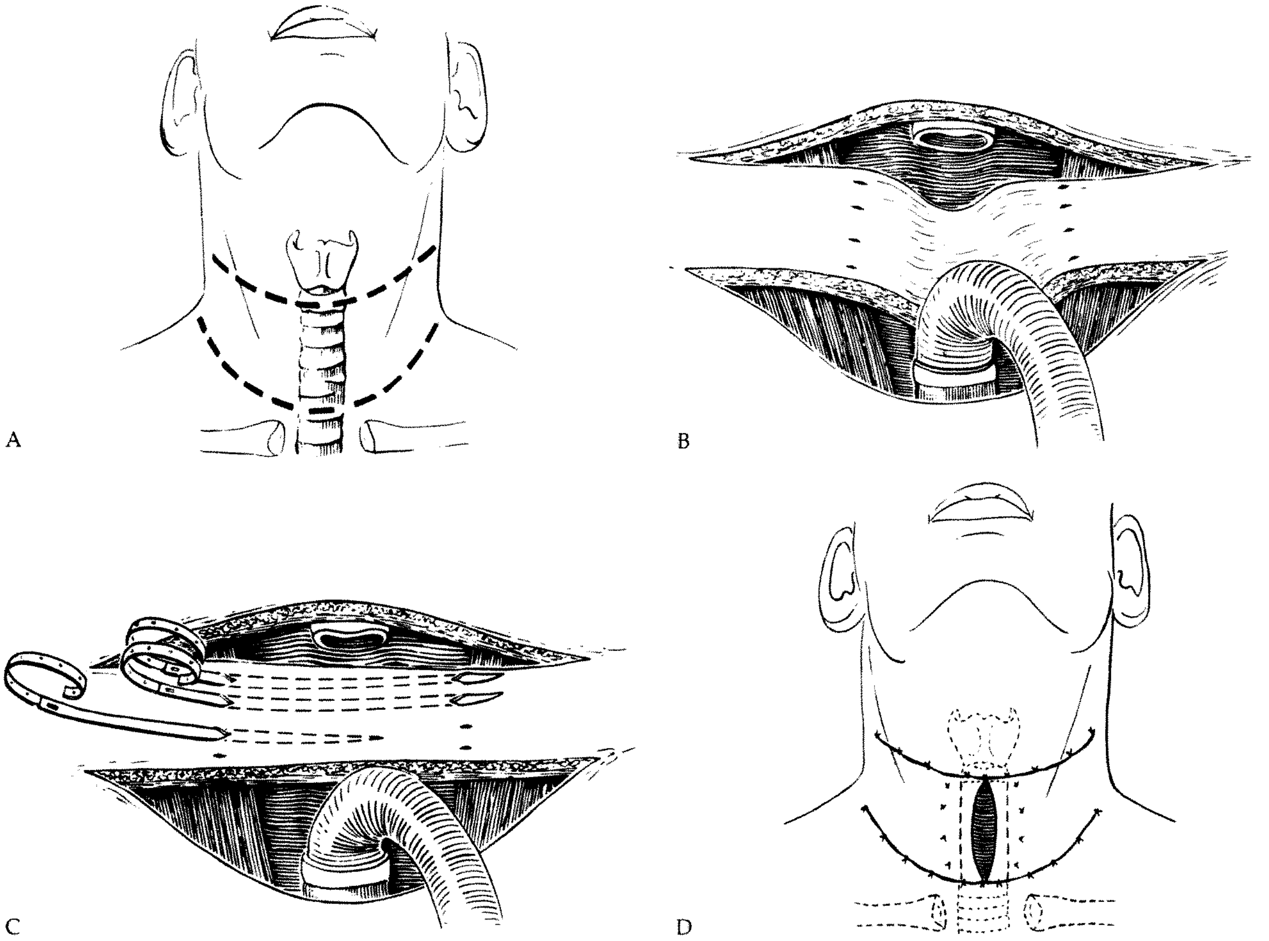

Fig 4. Cutaneous reconstruction of the trachea using skin and platysma splinted with inlying polypropylene rings. A. The bipedicled flap. B. The flap lying in the defect. C. The rings being inserted between skin and platysma. D. The interposed replacement. In a final stage, the anterior defect was closed. (Reproduced with permission from Ann Surg 1965;162:374.)

cess the development of carinal reconstructive techniques followed in the operating room, as I was secure in the knowledge that the basic elements of the operation were dependable. Gradually a systematic approach was developed for the various lesions requiring carinal resection and reconstruction [13].

I suspect that had the first case not succeeded, I might have seriously questioned the entire project. Two further successful transthoracic reconstructions for tumors followed the first case. One patient had squamous carcinoma of the lower trachea. Years later he had a lobectomy for a second squamous cancer and even later he underwent coronary bypass operation. The other had a large squamous papilloma. A few cutaneous tubes were fashioned before later information made it clear that they were rarely necessary [14].

In 1964 Dr Henning Pontoppidan of our Respiratory Intensive Care Unit introduced me bronchoscopically to the terrible destruction caused by cuffs on tubes in the trachea. I saw broken and protruding rings in the trachea of a patient who was still being ventilated. It wasn't too long after that that a patient was readmitted who had been ventilated successfully for toxic ingestion. She now had severe airway obstruction and bilateral basilar pneumonia. She was the first patient whom I treated surgically for postintubation stenosis (January 1965) (Fig 7). Her recovery was uneventful [14]. I would now be critical of treating a patient in this way. Today, she would have her stenosis dilated, the pneumonia would be cleared with medical treatment, and then elective resection would be done. Further, resection would be done from the anterior approach without opening the pleura.

A number of patients appeared with stenotic lesions of the trachea after intubation and ventilation. Many lesions were in the upper trachea. Stomal stenosis was recognized and differentiated from cuff stenosis. It was clear that the work that we had done on mobilization in the chest had little pertinence for these patients. I therefore returned to the dissecting room aided by Dr John Mulliken, a surgical resident. We selected an approximation tension (1,000 to 1,200 g) that was within what seemed experimentally to be a safe level and then determined, with the patient's neck in flexion (15 to 35 degrees), what length of trachea might be removed [15]. As a fall-back position might be necessary, we added to this the amount that might be gained additionally by intrathoracic mobilization, if the ends could not otherwise be brought together safely (Fig 8). This was somewhat theoretical as

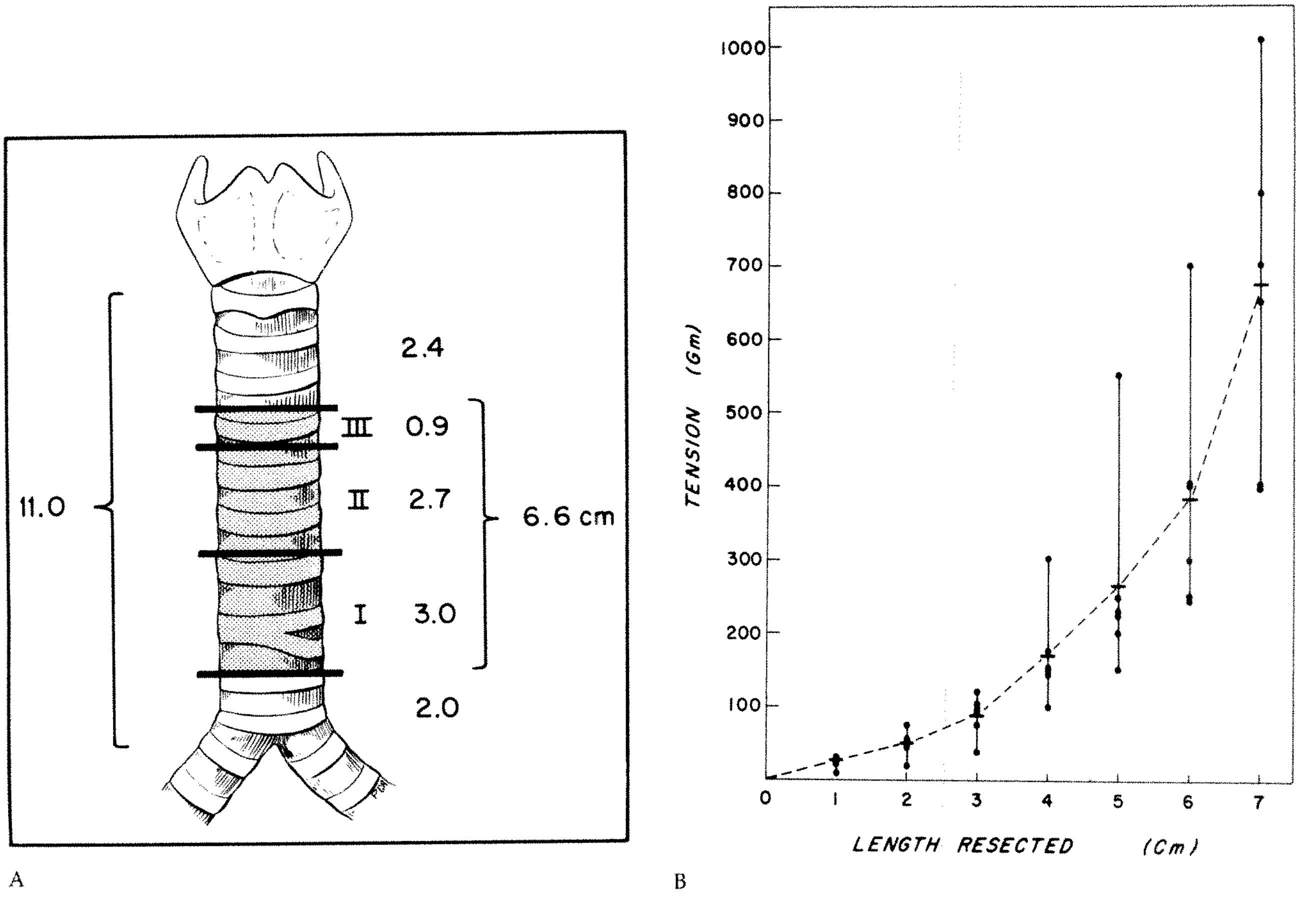

Fig 5. A. Diagram of the average amount of trachea that can be removed by steps in mobilization and still permit end-to-end anastomosis. I. Right hilar dissection and division of pulmonary ligament. II. Division of left main bronchus at carina and reimplantation. III. Dissection of pulmonary artery and veins from pericardium. In actual clinical use the right hilar dissection was followed by intrapericardial mobilization. Only rarely was the drastic step of bronchial reimplantation used, in view of the potential for complications. (Reproduced with permission from Ann Surg 1965;162:374.) B. Tension required for approximation after removal of successive segments of trachea. (Reproduced with permission from J Thorac Cardiovasc Surg 1964;48:741.)

many patients who had postintubation strictures had poor pulmonary reserve and would not tolerate transthoracic procedures. The approximation afforded by cervical flexion even greater than this also made cutaneous tube reconstruction unnecessary.

It is embarrassing to admit that it was only in connection with mobilization of the upper trachea that I realized how much cervical flexion could contribute to intrathoracic tracheal resection and reconstruction. The obvious is often only obvious after you have recognized it. Later I used the adjunct of laryngeal release for upper tracheal reconstruction, borrowing this from the otolaryngologists, moving from the thyrohyoid release of Dedo and Fishman [16] to the suprahyoid release of Montgomery [17]. It became evident that close communication with otolaryngology was necessary as the airway surgeon moved upward in the trachea. Disease does not tidily respect our anatomical and jurisdictional boundaries.

A gratifying aspect of this early work was my meeting a Canadian thoracic surgeon who also had strong interests in the trachea at the meeting of the American Association for Thoracic Surgery in Montreal in 1964. Up to that time I had the feeling that I was working in something of a professional vacuum. Almost no one in thoracic surgery seemed the least bit interested in the problems of airway surgery. It was a delight therefore to find that Griff Pearson was working actively with these same problems (Fig 9). Through subsequent years we developed a close relationship and always spoke freely and extensively of our observations, problems, and solutions to matters involving the trachea. I gained a great deal from this interchange. I hope it was mutual. We even managed to extend these seminars to include a few trout fishing expeditions. In casting a trout fly there is no question that I was the pupil.

Postintubation stenoses rapidly became the dominant group of cases. They came from all over, requiring only that patients survive ventilator therapy and that the diagnosis be made. There was considerable confusion and no shortage of theories about the origin of these lesions. It was essential to understand the pathogenesis of the lesions if we were to make any headway in their prevention. As a first step, I elected to look at the trachea of every patient who had been on a respirator who reached the autopsy room. Fortunately, the surgical resident assigned to pathology was a bright young man who eagerly ac-

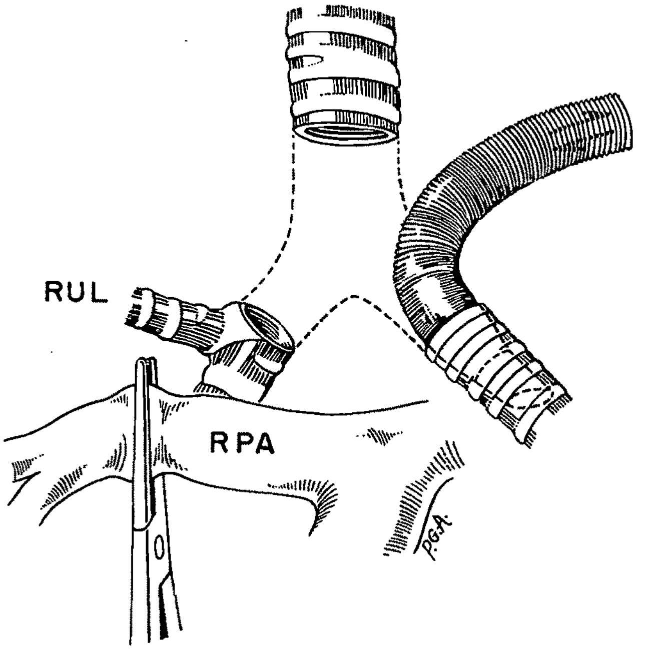

Fig 6. Our first tracheal reconstruction, which proved to be carinal. Reconstruction was accomplished by suturing the right main bronchus to the trachea and implanting the left main bronchus into the low lateral trachea. Temporary occlusion of the right pulmonary artery (RPA) eliminated perfusion of the unventilated lung. (Reproduced with permission from Ann Surg 1963;158:889.)

cepted my proposal that he take on this project with me. In no time at all he did a superb job of collecting and ordering these specimens (Fig 10). We developed an episodic, but complete picture of the pathological evolution of the injuries, concluding that the most important factor in etiology was pressure necrosis [18] (Fig 11). That promising young resident was Joel Cooper (Fig 12).

Our observations confirmed and extended like observations in Europe [19] and correlated with clinical observations [20, 21]. An interesting sidelight is that these lesions had gone largely unnoticed by pathologists. It is an example of the trap that we see what we expect to see. More positively, it is an example of how surgery repays its debts to anatomy, physiology, and pathology. The surgeon's project-oriented approach seeks specific information about a defined problem, often for a pragmatic goal. In so doing we make observations less likely to be made by our colleagues in other disciplines who view a system, an area, or a disease more generally.

An earlier example of this same motivation was our need to know the blood supply of the cervical trachea. When Dr Miura and I turned to the anatomy books, information was scant. We therefore did a series of injection studies that defined the patterns of blood supply to the upper trachea from the inferior thyroid artery [22] (Fig 13). Later, Salassa, Pearson, and Payne [23] completed a classic study of tracheal blood supply.

Dr Cooper and I decided to reproduce postintubation stenosis lesions, if possible, in an experimental animal, in part to confirm the thesis that pressure necrosis was the single most important cause of tracheal erosion and subsequent stenosis but also to provide a model that might be used to study methods of preventing the lesions. The lesions were reproduceable. Indeed, experimental dogs incurred these lesions in 100% of cases (Fig 14), just as they responded to our concept of a low-pressure, large-volume cuff in 100% of cases [24] (Fig 15).

It is an interesting commentary on the initiative of industry that it took more than a year to find a company willing to embark on production of a low-pressure cuff. Once this cuff had been produced and its safety proved, a randomized series of patients soon demonstrated clearly that our low-pressure cuff eliminated tracheal cuff stenosis [25] (Fig 16). This model was one of the prototypes of the cuffs that we all now use. The original cuff was made of latex which, because of extension characteristics, simply does not produce cuff injury. Ironically, it is no longer manufactured because of cost considerations having to do with shelf life and bonding of latex to plastic. Hence, all cuffs currently in use are plastic. These are usually safe when used as directed, but because attendants do not always follow directions and because the extension characteristics of plastic are different from latex, tracheal stenoses continue to be produced due to overinflation. These serve to teach residents the techniques of tracheal resection and reconstruction.

I like to think there may have been another benefit from these experiments. It is presumptuous for a teacher to take credit for a pupil's innate abilities and industry. I do, however, take considerable satisfaction in the fact that this work was Joel Cooper's introduction to research and, if nothing else, may at least have "hooked" him in the way of the investigator.

I began to see children with tracheal stenosis. I was uncertain whether the techniques developed in adults would work equally well in children. Although parallels could be drawn with coarctation of the aorta and bowel repair, the questions were unanswered whether tracheal anastomosis in infancy would grow proportionally with the child and whether delicate juvenile tissues would withstand tensions used in adult tracheal surgery. With the meticulous and painstaking help of Dr Masazumi Maeda, then from the University of Osaka and now professor of surgery at Kagawa University, and Dr Yahiro Kotake, these problems were analyzed in puppies. The facts that emerged were of practical use. First, the anastomoses, if done properly, did grow to 80% of normal [26]. Second, the juvenile trachea withstood tension less well than that of the adult [27] (Fig 17). We also explored methods that could be used to diminish tension [28]. This information was applied clinically [29]. A general rule may be enunciated that the average adult trachea can withstand resection of approximately one half of its length, but the juvenile trachea can withstand resection of no more than a third before problems based on tension may occur.

I shall not prolong what would become a tedious recital of the many tracheal problems with which we have attempted to deal. We should consider, however, that 30 years ago a lecture on tracheal surgery would have consisted largely of a description of the problems of tracheostomy with a few comments on ad hoc solutions to

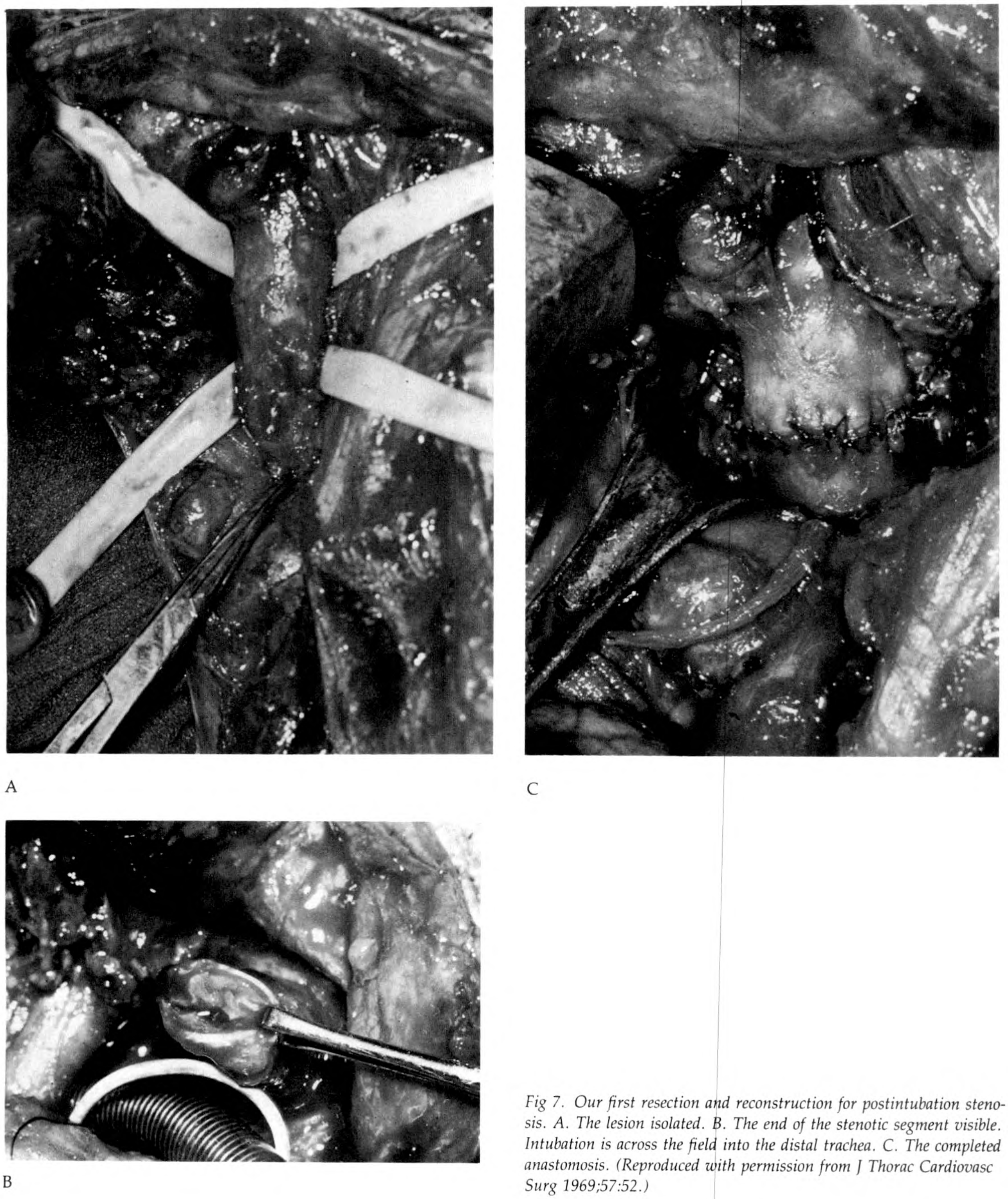

Fig 7. Our first resection and reconstruction for postintubation stenosis. A. The lesion isolated. B. The end of the stenotic segment visible. Intubation is across the field into the distal trachea. C. The completed anastomosis. (Reproduced with permission from J Thorac Cardiovasc Surg 1969;57:52.)

the difficult matter of rare tracheal tumors. Now there is almost too much to discuss. Let me simply enumerate some of the problems that appeared over the last decades and note where we stand in their management. Most of these problems were not taken to the laboratory. They were seen clinically, and the solution lay in the operating room, using principles of tracheal surgery that by now had become established. This illustrates a general course of surgical development. Once basic principles are established and their application worked out, extensions may safely follow without always needing to recapitulate prior experimental work.

Evolution of techniques of carinal reconstruction has already been noted [13]. These were systematically de-

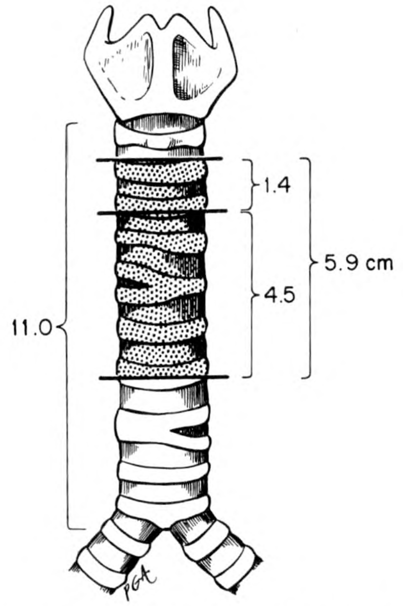

Fig 8. The amount of upper trachea that can be resected and still permit primary anastomosis under 1,000 to 1,200 g of tension was found to be 4.5 cm. Intrapericardial dissection added an additional 1.4 cm. (Reproduced with permission from J Thorac Cardiovasc Surg 1968;55:418.)

scribed in 1982 (Fig 18). Prior to that, in 1978, experiences with management of 28 patients with tracheal tumors, primary and secondary, offered hope for long-term survival with adjunctive irradiation even in patients with squamous carcinoma and adenoid cystic carcinoma of the trachea [30]. By 1987 127 primary tumors and 48 secondary tumors had been resected. Follow-up study is now in progress.

The other major area of tracheal reconstructive surgery was updated in 1979 with a detailed report of the types of lesions resulting from ventilation, the selection of treatment, techniques, and results, with overall good or satisfactory results in 93% of 203 patients [31]. By 1988 the number of postintubation patients resected was greater than 400. It is somewhat discouraging that these lesions continue to be seen despite the early acquisition of so much information on their prevention.

Tracheoesophageal fistula that occurs from erosion by a high-pressure cuff through the apposed membranous tracheal wall and the anterior wall of the esophagus usually occurs in conjunction with a foreign body, namely a feeding tube, in the esophagus. The common wall is pinched between the esophageal tube and a tracheal cuff. Consideration of the pathology and response of the tissues cautioned withholding repair until the patient was off the respirator. Single-stage repair with interposition of normal tissue between the two suture lines followed [32] (Fig 19). Equally important is the prevention of fistulas by avoiding prolonged use of foreign bodies in each of the adjacent aerodigestive tubes.

Tracheoarterial fistulas, caused either by erosion of a high-pressure cuff or tube tip through the anterior wall of the trachea into the innominate artery or, more commonly, by erosion by a tracheostomy tube lying against the innominate artery due to a low tracheostomy, are managed by the excision of the affected artery and appropriate management of the trachea depending on which of the two etiologies is involved [33]. Again, the emphasis is on avoidance. A properly placed tracheostomy (at the level of the second and third rings) will not produce these fistulas.

The very difficult problem of subglottic stenosis, which affects the subglottic portion of the larynx as well as the upper trachea, has been managed with considerable success by a single-stage operation [34] (Fig 20), not dissimilar to that pioneered by Couraud and associates in Bordeaux [35] and by Bryce, Pearson, and associates in Toronto [36, 37]. Thus, the thoracic surgeon has invaded the domain of the otolaryngologist, but only because the multiplicity of often multistaged procedures previously used for these lesions has failed to give acceptable results.

The complications of tracheal surgery and their prevention were discussed in detail in 1979, with the invaluable assistance of Drs Piero Zannini and Fabrizio Michelassi [38]. This analysis provided a sound guide to reduction in incidence of complications as well as to their treatment. Dr Luciano Landa presented our experience with the use of Montgomery's T-tube in tracheal surgery [39].

On rare occasions, either for potential cure or for

Fig 9. Dr F. Griffith Pearson, the first head of the Division of Thoracic Surgery, Toronto General Hospital. His approach to tracheal surgery was systematic, and he made special contributions to understanding the etiology and the surgical management of postintubation lesions.

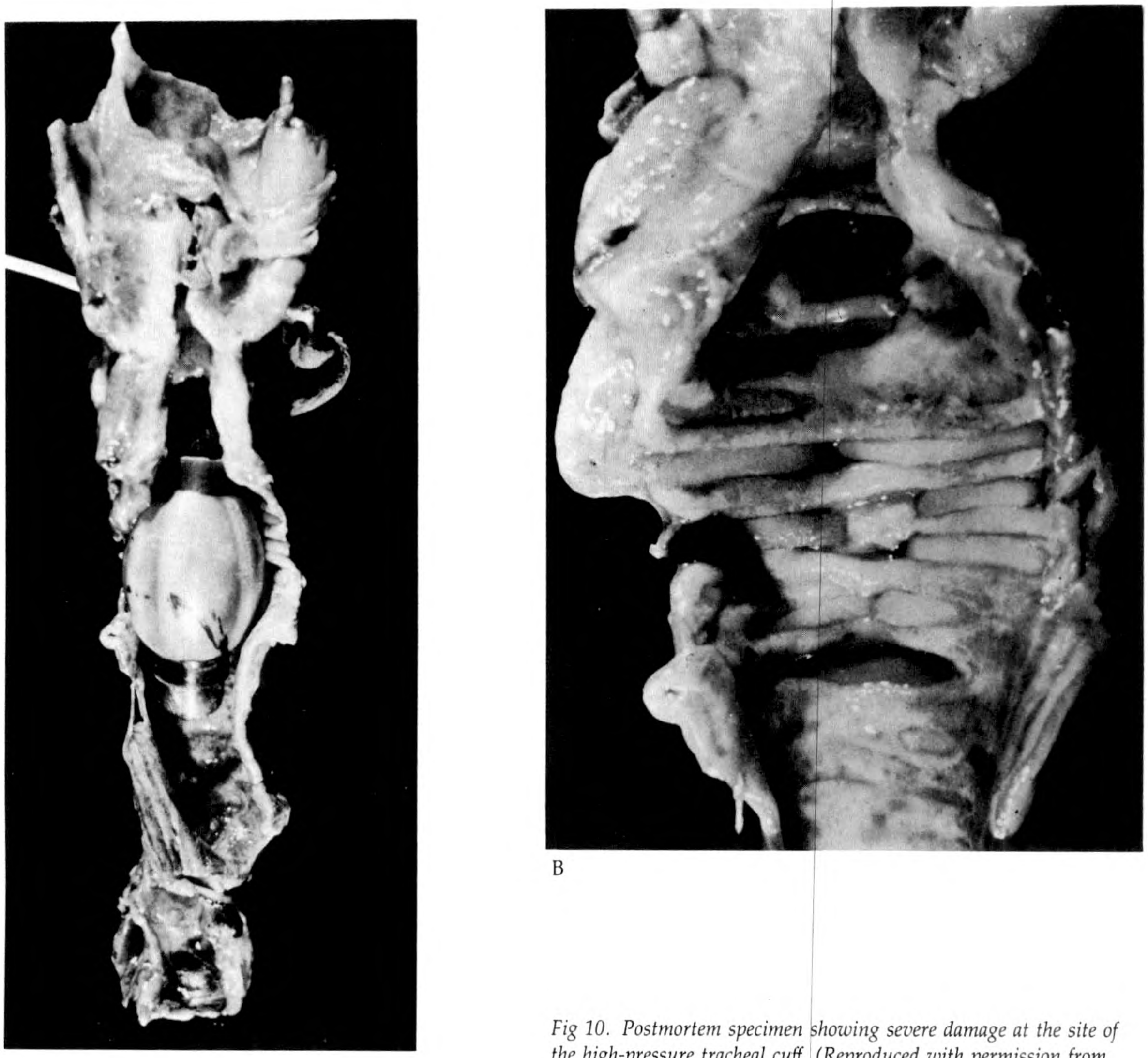

Fig 10. Postmortem specimen showing severe damage at the site of the high-pressure tracheal cuff. (Reproduced with permission from Ann Surg 1969;169:334.)

palliation in long-standing lesions, cervical mediastinal exenteration is necessary. This consists of the en bloc removal of larynx, trachea, pharynx, esophagus, and thyroid into the upper mediastinum with, most often, reconstruction of esophagus with stomach or colon and establishment of a mediastinal tracheostomy after partial removal of the sternum. The principle was established long ago that the surface must be brought down to the stump of the trachea because there is no way that the trachea can be pulled up to the normal surface contour of the body. Drs William Waddell and Bradford Cannon at the Massachusetts General Hospital devised a method of crossed skin flaps to produce a tube that reached the trachea [40]. Nonetheless, hemorrhage continued to be a troublesome and often lethal complication in cases in which healing was not perfect. I initially attempted to solve this problem by simplifying the approach, using a large bipedicled flap of skin dropped into a mediastinum that had been made accessible by removal of a bony plaque superiorly and anteriorly [41]. Despite initial success this technique proved still to be subject to the complication of major hemorrhage. This seems now to have been solved by selective division of the innominate artery under operative monitoring after appropriate preoperative study, and by bringing the omentum substernally into the mediastinum and neck to protect the arteries and esophageal closures [42] (Fig 21).

An unsolved problem of airway surgery, namely, resection and reconstruction of an airway that has previously received high-dose irradiation, has been similarly approached. Although this problem is not completely solved, in 6 of 7 patients in whom omentum was brought up to provide neovascularization and fibrogenesis after remote irradiation, healing has been attained. Formerly I would not have dared to operate on these patients.

During these decades surgeons have carefully extended the role of tracheal resection to some secondary tumors. Notable has been the use of carinal resection with pneumonectomy pioneered by Robert Jensik and associates [43] for selected patients with bronchogenic carcinoma. We have done our share of these and have advocated reimplantation of the lower lobe where possible. I have

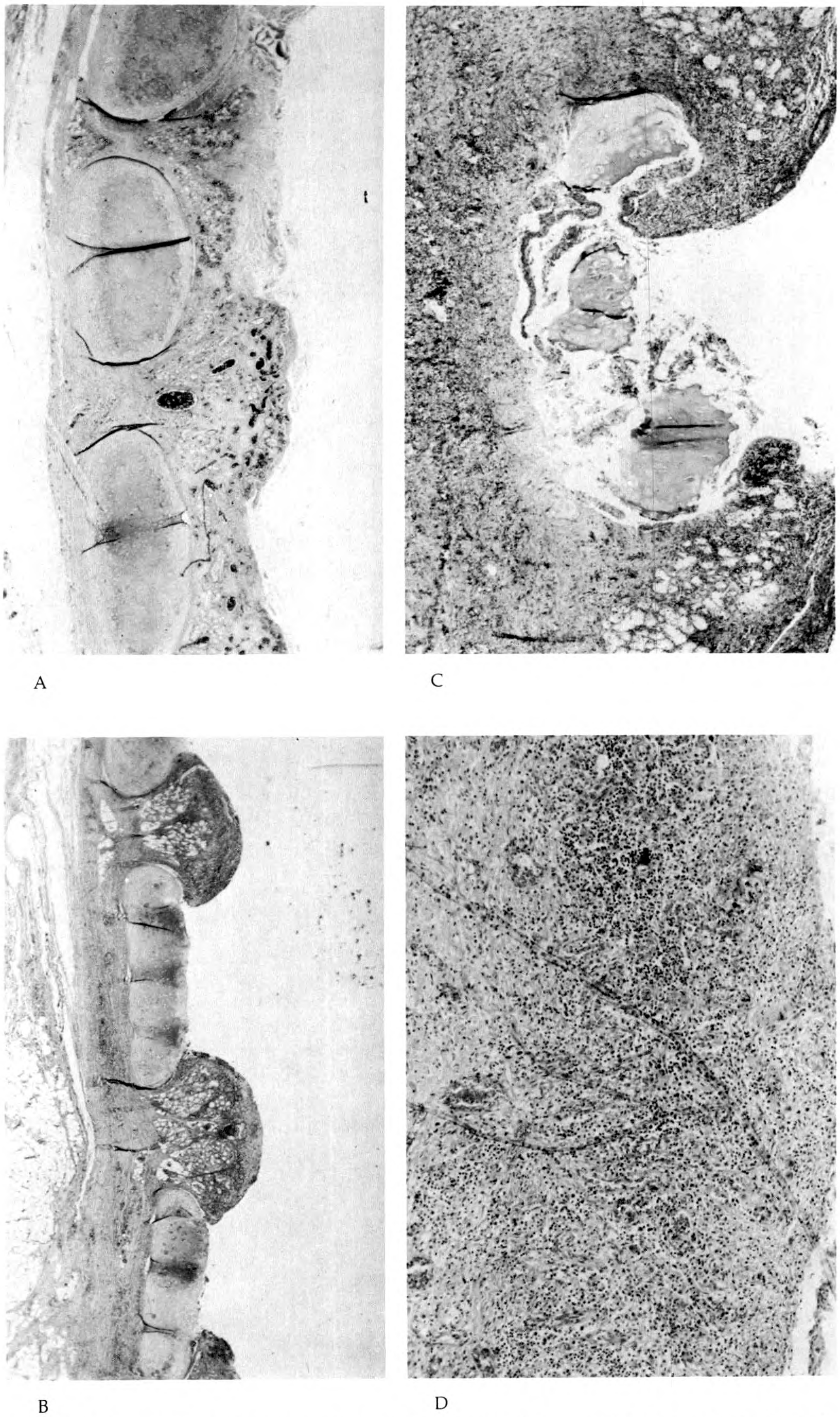

Fig 11. Microscopic study of the evolution of tracheal destruction under cuff pressure. A. Damage of the mucosa. B. Erosion to the cartilaginous surface. C. Cartilaginous destruction. D. Tracheal wall replaced by inflammatory granulation tissue.

also believed for some time that the surgeon who treats thyroid neoplasia, particularly locally invasive differentiated carcinoma in the older patient, has stopped short of fulfilling the basic tenet of treatment—removal of all local disease to prevent airway obstruction. Removal of the lower portion of the larynx and upper trachea in such cases has given promising results [44] (Fig 22). Optimal results are obtained in patients in whom such an operation is done initially or soon after the first operation. Unfortunately, this is often not the case. The airway surgeon must extend his work into areas that are not ordinarily the domain of the thoracic surgeon. The thoracic surgeon is best prepared to handle the total problem. Perhaps it is a caution against well meaning suggestions to truncate the general surgical background of thoracic surgeons. I say this not only with regard to the ability of the surgeon to accomplish specific procedures, but also because the evolution of general thoracic surgery in the future is unknown. I believe this anecdotal story of the recent evolution of tracheal surgery documents not only the specific value of an education in general surgery, but, to cite a caution by Edward Churchill, the value of a general education in surgery [45].

It is not unexpected in a Presidential Address that respectful obeisance be made to one's personal demigods—great teachers. I've spoken of Edward D. Churchill (Fig 23), truly one of the founders of thoracic surgery, great in his conceptions and in his surgical and pedagogical accomplishments, to whom I owe great debts, direct and indirect [46–49]. Richard H. Sweet (Fig 24), perhaps the all-time master of esophageal surgery, provided another model. None who observed his surgery hoped to equal it, but his elegance and precision were the standards to which we aspired [50].

Fig 12. Dr Joel D. Cooper. After residency and fellowship at the Massachusetts General Hospital, Dr Cooper went to the Toronto General Hospital, where he succeeded Dr Pearson as head of the Thoracic Surgical Division. There he pioneered successful lung transplantation. He now heads the Thoracic Surgical Division at Barnes Hospital, St. Louis.

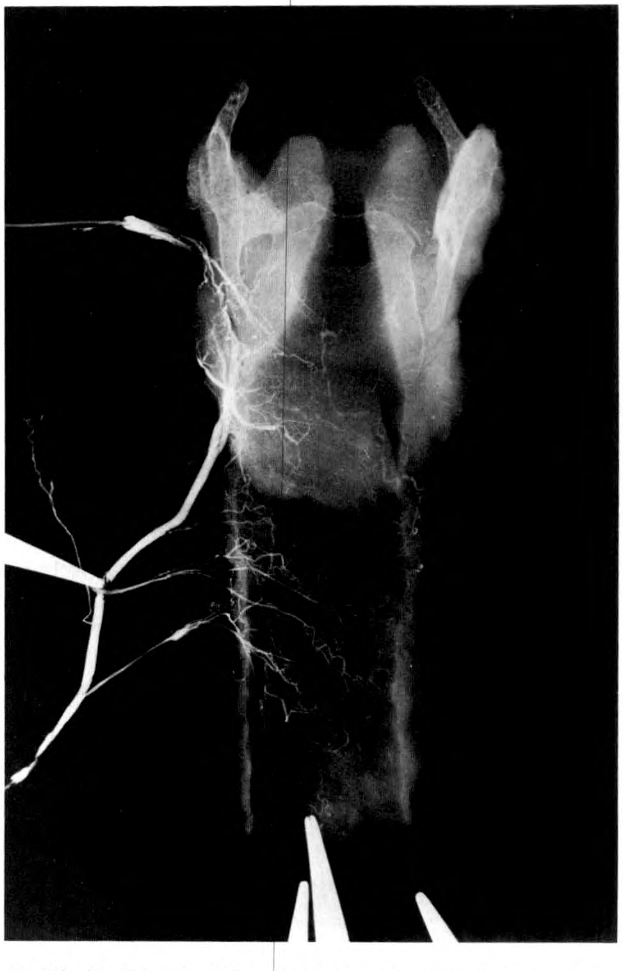

Fig 13. The blood supply of the upper trachea, demonstrated in roentgenograms of dissected specimens with barium sulfate injection of the inferior thyroid artery. (Reproduced with permission from Surg Gynecol Obstet 1966;123:99.)

Throughout all of this work it has been a particular pleasure to enjoy the fellowship of a relatively small number of thoracic surgeons around the world who are profoundly interested in the trachea. I have already mentioned my relationship with Dr F. Griffith Pearson. I particularly wish to acknowledge the outstanding contributions by Mikhail Perelman of Moscow (Fig 25) and Henri Eschapasse of Toulouse (Fig 26). Exchanges of opinion with these superb and innovative surgeons have been most valued over many years.

Surgical efforts are always intertwined with other disciplines. Each contributes to the other's development. Thus, as tracheal work evolved, Benny Geffin and then Roger Wilson took on the problems of anesthesia in

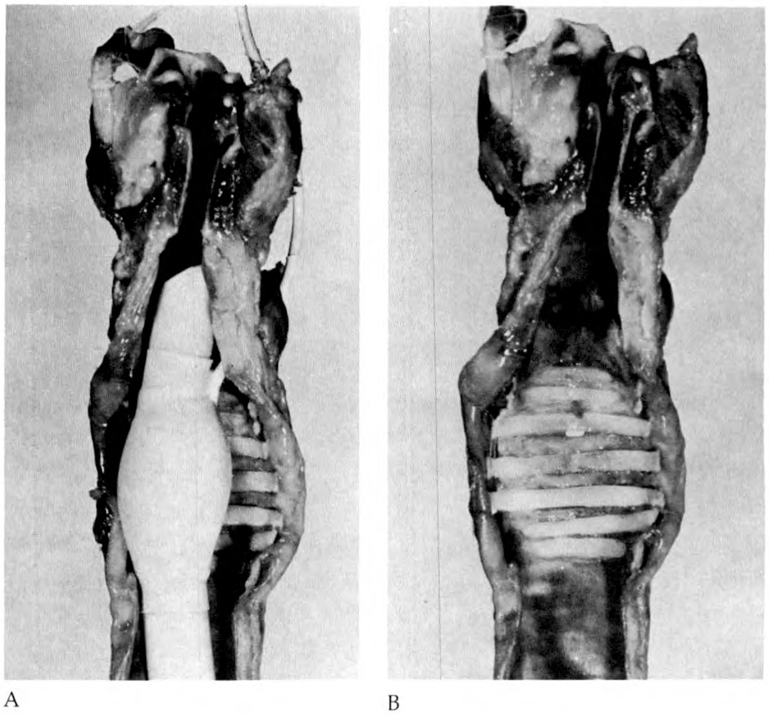

Fig 14. Experimental production of tracheal erosion from standard high-pressure cuffs in the canine trachea. At seven days the lesions mimicked those seen in humans. (Reproduced with permission from Surg Gynecol Obstet 1969;129:1235.)

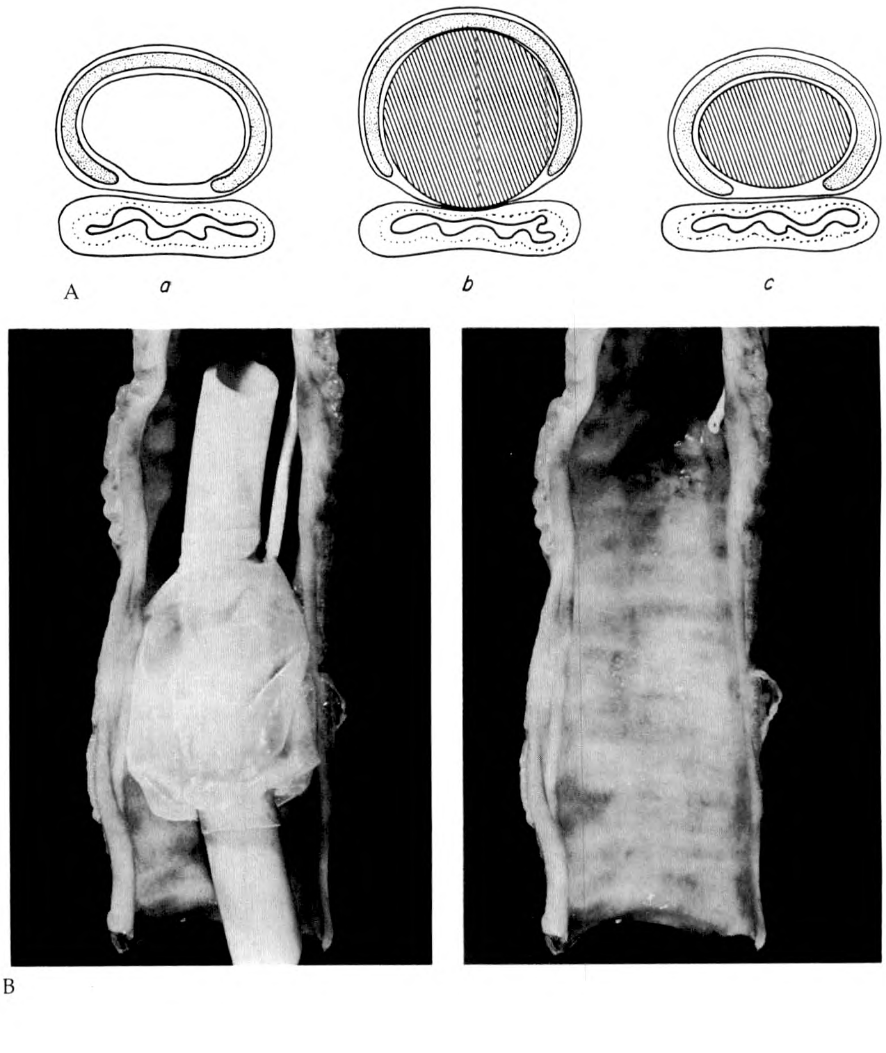

Fig 15. A. (a) Diagram of the sealing of the trachea by a high-pressure cuff (b), which has deformed the trachea as it expands to occlude the lumen, and by a low-pressure cuff (c), which has flowed out to conform to the tracheal lumen and seal it before the pressure rises. B. Appearance of the dog's trachea (right) after 13 days of exposure to a large-volume, low-pressure balloon cuff (left). (Reproduced with permission from Surg Gynecol Obstet 1969;129:1235.)

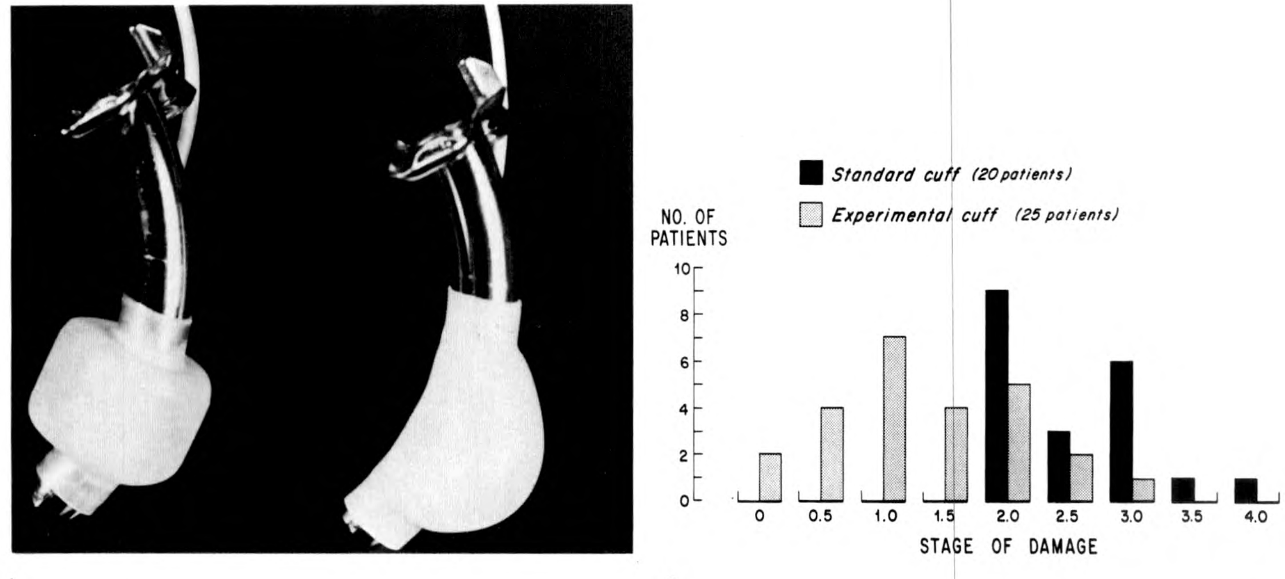

Fig 16. A. The experimental latex large-volume, low-pressure cuff (left) compared with a standard Rusch cuff (right), both mounted on standard Jackson tracheostomy tubes. B. Damage to the human trachea from standard high-pressure and experimental low-pressure cuffs. The slight degrees of damage seen with the low-pressure cuff were not in ranges that led to stenosis. (Reproduced with permission from J Thorac Cardiovasc Surg 1971;62:898.)

tracheal surgery [51, 52]. If there is any area of surgery in which the anesthetist and surgeon must be in close and continuous communication, this certainly is it. Residents in anesthesia at Massachusetts General Hospital look forward to their rotations on thoracic surgery in part to deal with complex intrathoracic airway reconstructions. Two radiologists at the Massachusetts Eye and Ear Infirmary, first Dr Alexander McMillan, Jr, and then Dr Alfred Weber, standardized and simplified the radiology of the larynx and upper trachea in a way that defines the lesions precisely without the necessity for contrast or exotic studies [53, 54]. Dr Theresa McLoud and her associates have carried on a similar characterization of the lower trachea and carina [55]. Obviously there are parallels also in the work of the pulmonary pathologist Dr Eugene Mark [56] and of our pulmonologists [57]. These are examples of the web that exists in all of our therapeutic efforts. No one would dare to undertake carinal reconstructions without the support of an expert nursing service and intensive care unit staff as well as these other specialists.

I must state the obvious—not all problems of airway surgery are solved. Two in particular are insistent. The first is that of subtotal replacement of the trachea. With the techniques that have evolved, a need for subtotal replacement arises in only a very few patients in a year. The key example is that of a longitudinally infiltrating adenoid cystic carcinoma without extensive mediastinal or laryngeal invasion. Although episodic successes have been reported with a variety of foreign prostheses from the beginning of tracheal surgery [4], most still founder on a biological reef. When foreign material is implanted into the body in contact with an epithelial margin, a chronic nonhealing ulcer results. The usual results are, after a time, obstruction due to chronic granulations or erosion of major blood vessels with fatal hemorrhage. None of the prosthetics currently available have triumphed over these problems to a degree that makes them safe in general usage. It is particularly the case in the lengthy resections for which they are truly needed. A new concept is required. All currently successful surgical prosthetics

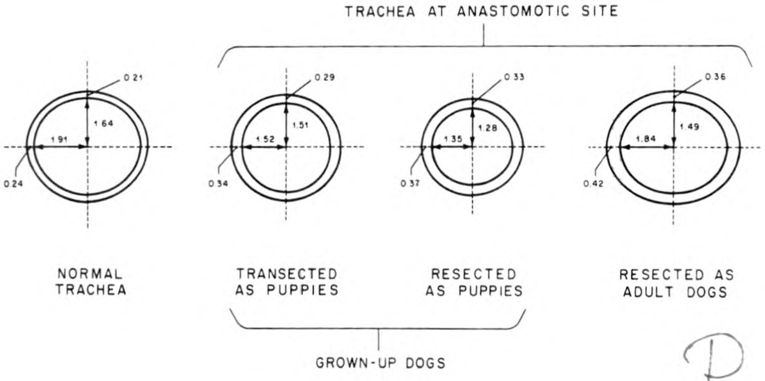

Fig 17. Tracheal cross-section measured at anastomotic sites in the normal adult dog, in dogs transected as puppies and in dogs who underwent resection as puppies (at the grown-up stage in both), and in dogs with resection as adults. These studies demonstrated that the juvenile trachea grew satisfactorily, but was influenced by the tension resulting from resection. (Reproduced with permission from J Thorac Cardiovasc Surg 1973;65:658.)

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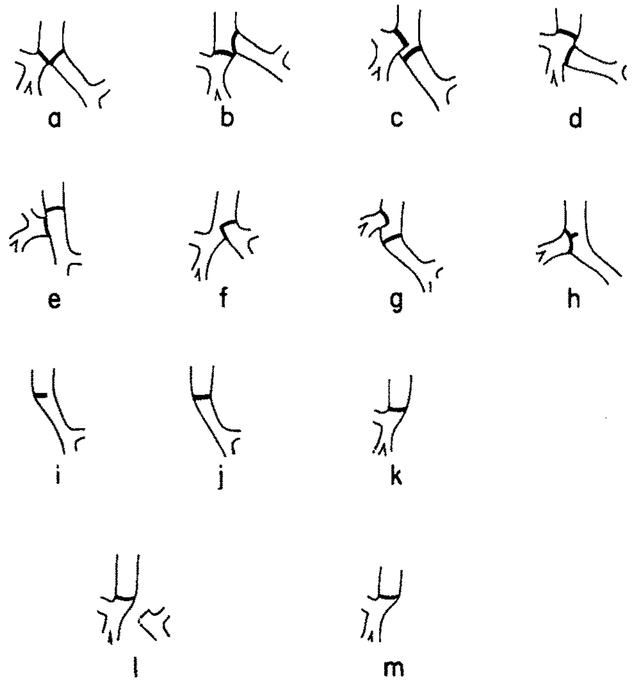


Fig 18. Types of primary reconstruction performed in the first 31 carinal resections. (Reproduced with permission from Ann Thorac Surg 1982;34:364.)

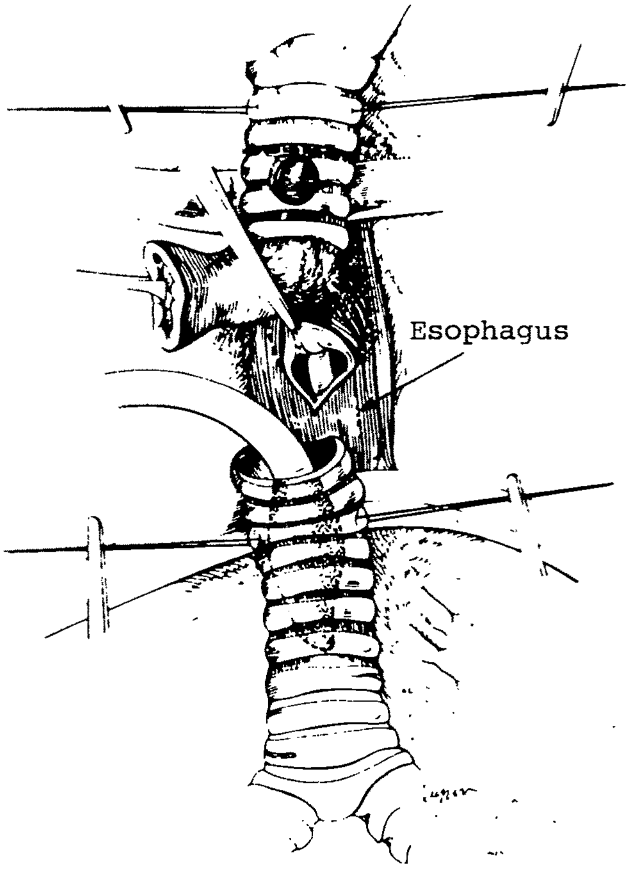
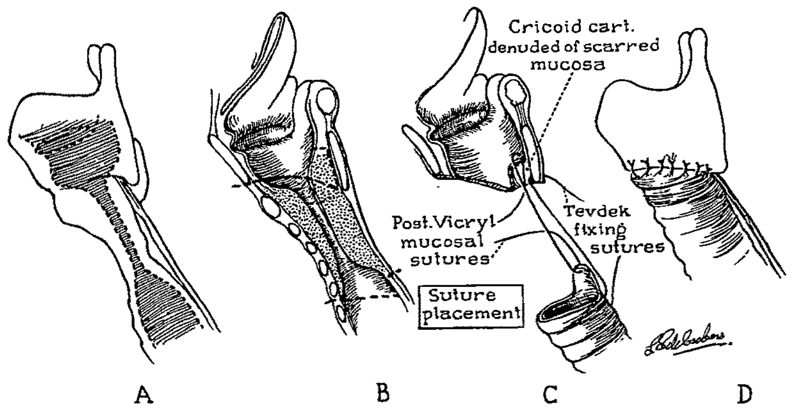


Fig 19. Single-staged repair of acquired tracheoesophageal fistula. The damaged tracheal segment is resected with the fistula. The esophagus is closed in layers, and strap muscle is interposed between it and the subsequently anastomosed trachea. (Reproduced with permission from Ann Thorac Surg 1976;22:112.)

(vascular, cardiac, and orthopedic) are embedded in mesenchyme, which is potentially sterile. There are no examples of prosthetics that are usually successful in the gastrointestinal tract, the genitourinary tract, or the respiratory tract.

Important also is the dependability of any technique. This is illustrated by the efforts a few years ago by Dr Joo Hyun Kim and I to create a complex prosthesis with the following characteristics: (1) a rigid tube, (2) autologous tissues, with good blood supply, (3) epithelial surface, and (4) anatomical mobility. In dogs we constructed a tube that consisted of a cylinder of cartilage formed from costochondral perichondrium wrapped around a stent. The epithelial lining of the tube was a buccal mucosal graft. The tube, constructed in stages, was based on an intercostal pedicle, which allowed it to be moved into the tracheal defect. It worked just fine in *some* of our experimental animals. On the other hand, more experiments failed than succeeded. Clearly this is not a procedure that one would ever attempt in humans. Indeed, we refrained from publishing the results despite the intriguing successes achieved. It is an old belief of mine that when 100% of experiments in animals succeed, there is a bare possibility that the procedure may work in humans. As the percentage of success in the experimental animals drops, the likelihood of a complex method succeeding in humans becomes remote.

Fig 20. Subglottic stenosis involving the lower larynx and upper trachea. A. The lesion. B and C. Resection includes the anterior subglottic larynx and the scarred mucosa overlying the cricoid plate. D. In the reconstruction, the flap of membranous wall resurfaces the cricoid plate and the cartilaginous trachea reconstructs the subglottic larynx. (Reproduced with permission from Atlas of General Thoracic Surgery, *Ravitch M, Steichen F, eds. Philadelphia: WB Saunders, 1988.)*



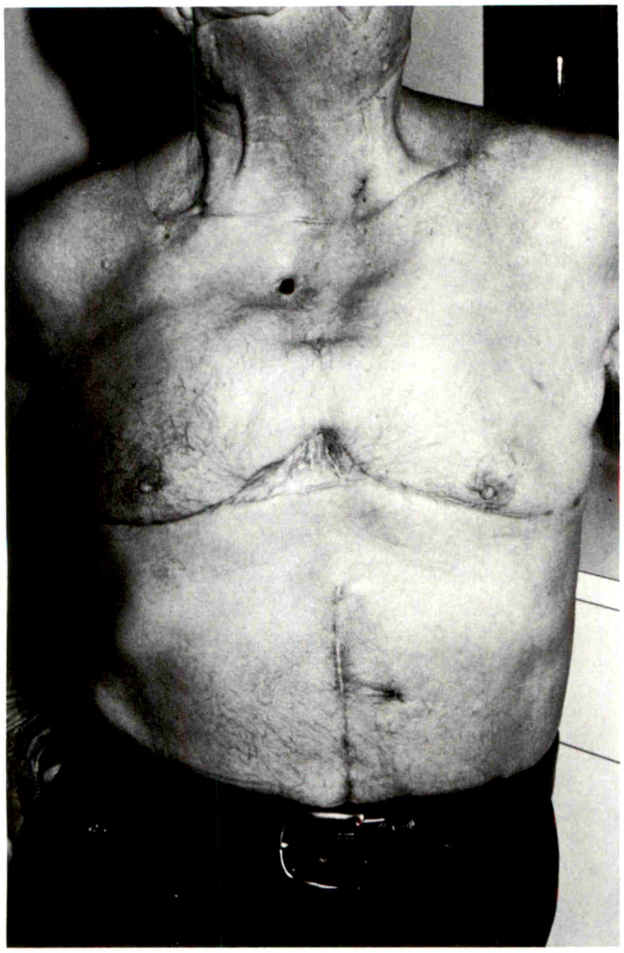


Fig 21. The final result from cervicomediastinal exenteration with mediastinal tracheostomy. The parallel incisions along the line of the clavicle and below the breasts are visible. The sternal defect may also be seen, with the end tracheostomy lying within the mediastinum. The colon or stomach and the omentum are advanced substernally.

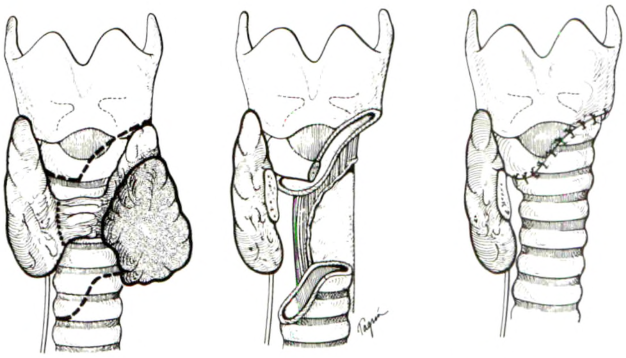


Fig 22. Aggressive local resection of differentiated thyroid carcinoma invading the airway. A portion of the lower larynx as well as the upper trachea has been excised with the tumor. Recurrent nerve was already paralyzed by the lesion on that side. The trachea is tailored to fit the laryngeal defect. A portion of esophageal muscular wall has also been removed. (Reproduced with permission from Ann Thorac Surg 1986;42:287.)

Another broad area of work in progress is treatment of what may loosely be catalogued as tracheomalacia. This includes a variety of malacic changes in the trachea, such as idiopathic diffuse loss of cartilage, expiratory collapse with broadening of the rings and membranous wall, and segmental malacia in postpneumonectomy syndrome. We have handled these and other cases surgically in numerous ways including the use of posterior splinting of the elongated membranous wall following the methods of Nissen, Herzog, and associates [58, 59], the use of circular polypropylene splints in patients with tracheomalacia due either to idiopathic causes or to compression by goiter, and a variety of procedures for the intriguing and complicated entity of airway obstruction following mediastinal displacement after right pneumonectomy (and its mirror image of left pneumonectomy with right aortic arch) [60]. There is much left to be done by the young surgeon interested in difficult problems of the airway.

What lessons may be learned from this surgical odyssey? Perhaps the lessons are largely a reaffirmation of platitudes. Our learning process in life is continuous. Experience sometimes heightens awareness of the true meaning of conventional wisdom previously accepted on an intellectual basis. Concepts then become something that we know with real understanding. I shall recite a few

Fig 23. Dr Edward Delos Churchill (1895–1972), John Homans Professor of Surgery at Harvard and Chief of the Surgical Services, Massachusetts General Hospital, pioneer in thoracic surgery, outstanding surgical educator, and a surgical scholar and humanist.

Fig 24. Richard Harwood Sweet (1901–1962), Associate Clinical Professor of Surgery at Harvard and Visiting Surgeon at the Massachusetts General Hospital, a master surgeon who, with Churchill, pioneered modern esophageal surgery. He reported clinical experience precisely and was an invaluable teacher for the resident surgeon and a founder of the Board of Thoracic Surgery. Photographed by Fabian Bachrach.

of these platitudes, perhaps better dignified as principles. (1) There must be a willingness to question and to reexamine conventional wisdom. Examples I gave at the outset were those of the "2-cm rule" for tracheal reconstruction and the often repeated statements that cartilage did not heal. The questioning must apply to one's own assumptions also. (2) An experience in scientific research, even in a remote discipline, helps to prepare the clinician for an analytical approach to problems. I hurry to add that the young surgeon must desire and seek such an experience. I do not believe that enforced labor in the laboratory will be productive or even educational. (3) Careful laboratory preparation to the extent that it is possible before the battle is joined in the operating room is clearly the safest and most valuable way to approach new surgical problems. (4) Willingness to return to the laboratory as further problems arise should be part of the surgeon's approach. (5) The surgeon should work within the laws of biology in devising new procedures. He must know what he can expect from tissue responses. Unless these can be modified as demonstrated experimentally, he must avoid wasting time and must work within these limits. (6) Sustained and persistent efforts are generally needed to make forward movement.

I must add a corollary to the last point, which I hope will not be misconstrued. In dealing with apparently simple, yet complex problems that are not frequently encountered, such as tracheal reconstruction, the best results for our patients will be obtained if the work is concentrated in special units where a continuing commitment has been made to this type of work. Bad results are part and parcel of difficult operations, but I continue to be appalled by disasters that I see occur in what should be a simple airway operation. These are often the results of procedures done without appropriate thought or preparation.

I believe that we can summarize the last 25 years of tracheal surgery much as one could summarize the first 25 years of pulmonary surgery, of esophageal surgery, and of cardiac surgery. In each case what appeared to be a difficult and relatively untried area of surgery was entered with considerable success. However, without in any sense derogating what has been done, we note that the strides made by the "buccaneer surgeons" in each case have been relatively easy conquests *in retrospect*. Further

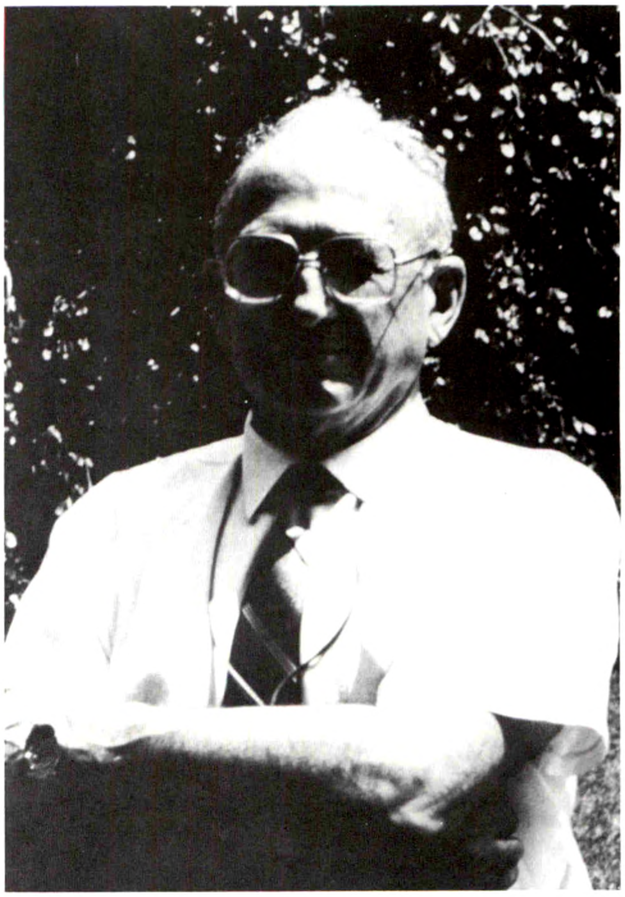


Fig 25. Professor Mikhail Perelman, Head of the Department of Thoracic Surgery of the National Centre of Surgery, Moscow, one of the world's most experienced tracheal surgeons. He is a skilled and innovative surgeon who has published many papers and three monographs on tracheal, bronchial, and pulmonary surgery.

Fig 26. Professor Henri Eschapasse of Toulouse (left) with Dr Pearson in 1981 before a meeting in Bordeaux. Professor Eschapasse has been especially interested in the treatment of tracheal tumors.

advances will require more sophisticated effort because the problems are more complex and more refined. Real advances may therefore be more difficult.

One of the most satisfying aspects of this personal odyssey has been to work with a succession of talented young residents. It is gratifying to see how easily the techniques of tracheal surgery may be transferred to the apt and willing pupil. A measure of the validity of an operation is that it may be taught successfully. From working with these extremely able young thoracic surgeons, I have every confidence that they and their peers will continue to change and improve thoracic surgery, however difficult the next stages may be.

I shall close with a few words directed to young thoracic surgeons. When I expressed an interest as a young surgeon in working in general thoracic surgery, I was cautioned by a distinguished thoracic surgeon, "Hermes, everything has been done in thoracic surgery." A few years later a noted British thoracic surgeon was escorted through the laboratory where I was working on our early tracheal experiments. He listened, looked briefly, and said only three words: "It won't work." Then he turned on his heel and left. Do not let us—your seniors—discourage you with such words or by pronouncements of immutable rules. Remain skeptical, work carefully and reasonably, and you may rewrite the rules—at least for a time.

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Introduction to the Sloan Lecture

Hermes C. Grillo, MD

President, The Society of Thoracic Surgeons

It is now my particular pleasure to introduce the first Herbert Sloan Lecture of The Society of Thoracic Surgeons. It is a dual pleasure: on the one hand, to give honor to the distinguished surgeon and admired colleague for whom the lecture is named, and on the other hand, to introduce the lecturer.

The Herbert Sloan Lectureship was endowed in 1984 by Little, Brown and Company and The Society at the time of Dr Sloan's retirement as editor of *The Annals of Thoracic Surgery*, a post that he had held from 1969 to 1984, as second editor of the journal. The Lectureship is a recognition and an accolade for a member of this Society who has contributed for many years with head and heart to the welfare of The Society. He served as our president, as he did also as president of the American Association for Thoracic Surgery.

Dr Sloan is a graduate of the Johns Hopkins Medical School, where he also completed his general surgical training. After a military interlude between 1944 and 1947 spent in the Far East, he trained in thoracic surgery under John Alexander and Cameron Haight. He remained at Michigan, where he moved steadily upward to become head of the Section of Thoracic Surgery from 1970 until 1985. In addition to his multiple scientific contributions, his heavy administrative and pedagogical role at Michigan, and the editorial duties noted, he gave much more to thoracic surgery. He spent many years as a director, vice-chairman, and secretary of the American Board of Thoracic Surgery. His honors are numerous and include the Distinguished Service Award of this Society. In 1984 a Festschrift volume of *The Annals* was devoted to Dr Sloan's honor. This lecture today is another recognition, Dr Sloan, of your many and continuing contributions to thoracic surgery.

Our first Sloan lecturer, Dr Joel D. Cooper, has moved in a geographically triangular pattern. In 1960 he came east from West Virginia to Harvard College, where he was a summa cum laude graduate in chemistry. He only managed a cum laude at Harvard Medical School, but I can tell you that's not especially easy. I met him when he came to the Massachusetts General Hospital as an intern in 1964. He gradually progressed through the interminable residency to completion in 1972. These years included also a period as senior registrar at the Frenchay Hospital in Bristol with Mr Ronald Belsey, a research fellowship at the Hammersmith in London, where he became familiar with John West's techniques, and a research fellowship in thoracic surgery at the Massachusetts General Hospital.

He then moved north to Toronto to the Toronto General Hospital. I was delighted to see him join Griff Pearson in that outstanding division, although I was regretful to have him leave the Massachusetts General Hospital. In 1978 he became head of the division at Toronto, and it was during these years that he performed the outstanding research and clinical work in lung transplantation that he is going to tell us about today. Lung transplantation really remained an idea until Dr Cooper and his associates made it a reality.

He has just recently completed a further leg of the triangle and moved west, though a bit further west than West Virginia, this time to St. Louis, where he heads the Thoracic Surgical Division in the Department of Cardiothoracic Surgery at Barnes Hospital, Washington University.

Before I turn the podium over to Dr Cooper for what I am sure will be a distinguished lecture, I must tell you that I recall a very concerned young resident coming into my office when he was midway to a career in general thoracic surgery. Joel got to the point quickly, as he always does. He asked whether he had selected a field that was going to disappear. "Look what has happened to the surgery of tuberculosis, the surgery of bronchiectasis, and the surgery of lung abscess. Am I," he asked, "going into a field that is going to vanish?" I assured him that there would be thoracic surgery and thoracic surgeons around for a good long time and that there always would be something for him to do in the field. I think time has proved that he has found something to do in the field of thoracic surgery.

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Lung Transplantation

Joel D. Cooper, MD

Section of Thoracic Surgery, Division of Cardiothoracic Surgery, Washington University, St. Louis, Missouri

It is a great privilege as well as a great honor for me to deliver the first Herbert Sloan Lecture (Fig 1) to this Society, and I am most grateful to Dr Grillo and The Society for this opportunity. In addition to our common interest in thoracic surgery, Dr Sloan and I have something else in common: we're both just country boys from the state of West Virginia—Dr Sloan from Clarksburg and myself from Charleston.

In honoring Dr Sloan we are honoring an individual who is recognized not only for his personal accomplishments, but more importantly for his devotion to teaching, training, and education. A surgeon's personal contributions are all too soon improved, outdated, irrelevant, or obsolete. What endures is the individual's approach to problem solving, to clinical practice, and to education, and the stimulating effect he has on the next generation. Dr Sloan continued the legacy of Drs John Alexander and Cameron Haight, added his own immense contributions, and devoted much of his career to ensuring that these traditions would be preserved and disseminated.

It was with these thoughts in mind that I sat down to prepare this lecture on lung transplantation and realized that the specifics of the material I was to present were less important than the approach to surgical research that made them possible—an approach taught to me by several teachers and mentors with whom I have been privileged to work. These have included our distinguished president Dr Hermes Grillo, who stimulated my interest in thoracic surgery and in thoracic surgical research, and my colleague and close friend Dr F.G. Pearson, with whom I have had the good fortune to work for the past 16 years before moving to St. Louis, where, I might say, the legacy of Evarts Graham is still very much alive. These individuals, like Dr Sloan, have exerted a major influence on the careers of other thoracic surgeons by virtue of the example, the motivation, and the guidance that they have provided.

My first introduction to surgical research was as a resident of the Massachusetts General Hospital under the guidance of Dr Grillo. There we sought to define the nature, the etiology, and the prevention of postintubation tracheal stenosis, which was then a not infrequent and often serious complication of uncertain etiology. Our laboratory was first the autopsy room, then the animal laboratory, then finally the clinical ward. I subsequently found this quote from the great surgeon William Halsted, which has become a favorite of mine: "The hospital, the operating room and the ward should be laboratories, laboratories of the highest order."

Fig 1. Dr Herbert E. Sloan.

My work with Dr Grillo in defining the nature of cuff injury to the trachea and developing a low-pressure cuff for its prevention is an example of one type of research, namely problem solving, or goal-oriented research. It is different and less sophisticated than the type of research that expands fundamental knowledge without a particular application in mind. I think the surgeon is particularly well suited for this first type of investigation. He can observe a clinical problem, take it to the laboratory, provide the motivation and drive to see it through, and apply his new knowledge back to the clinical arena. It may not require the type of expertise, training, and ability necessary for modern fundamental research, but it is an avenue whereby many surgeons have made, and can continue to make, important contributions.

I have put together a rough outline of the steps that, to

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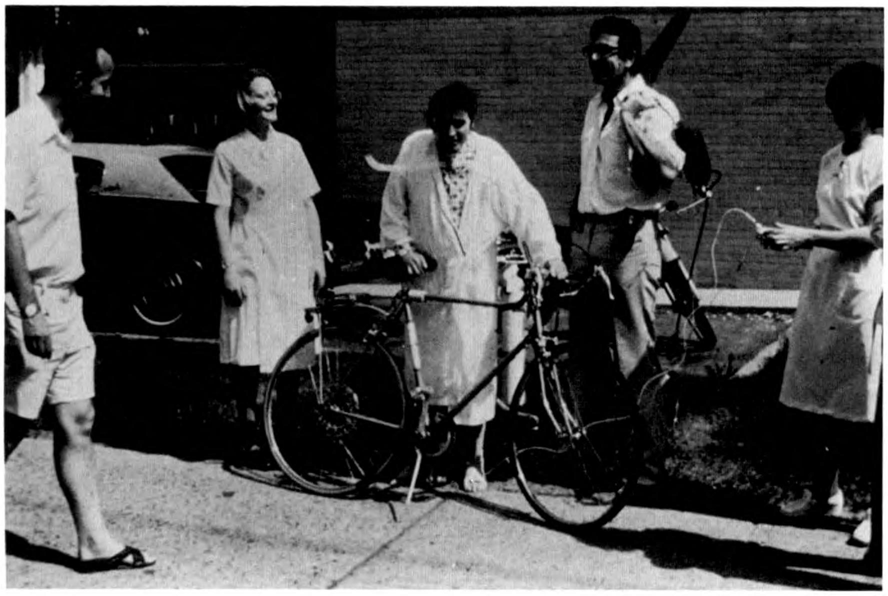


Fig 2. Nineteen-year-old boy in second week after a right lung transplantation for inhalation burns, surrounded by members of the nursing and medical team. The patient is receiving oxygen via a T-piece attached to a tracheostomy tube.

my mind, are important in pursuing clinically oriented research in the laboratory. First and foremost is the recognition that a problem exists, a problem requiring a solution. Second, there must be an interest or a motivation that propels the surgeon to seek a solution. The next step is detailed observation and documentation of the clinical problem to define its nature, combined with a review of the literature on the subject. Having a fundamental background before you begin the investigation is clearly important, bearing in mind Pasteur's dictum that "in the fields of observation chance favors only the mind that is prepared."

As surgeons we go to the laboratory and try to develop an animal model, a model that can be used under controlled circumstances, a situation that seldom exists clinically. The model will hopefully reproduce the type of problem that one has observed clinically. The next step is to experiment with the model to manipulate or alter factors one at a time in an attempt to reduce or eliminate the problem. Finally, if one has been fortunate enough to come up with some improvements, one can return to the clinical situation in an attempt to demonstrate that they can be applied and scientifically validated with a properly designed clinical study.

If the problem involves an anatomical or pathological problem, or the development of a new technique, the autopsy room is an invaluable resource—part of the hospital-laboratory to which Halsted referred. The great surgeon Billroth emphasized the importance of surgical practice on animals and cadavers prior to human application.

This, then, is the approach that I was taught and that my colleagues and I, along with numerous research fellows over the years, have applied to the area of lung transplantation.

Our initial venture in clinical lung transplantation was in 1978, some 30 years after the demonstration of lung transplantation in dogs by Metras [1] and 15 years after Dr James Hardy's initial lung transplantation in humans [2]. We performed a right lung transplantation in a young man who had suffered respiratory burns in a house fire.

Table 1. Human Lung Transplantation Chronology

Year	No. of Transplantations
1963	2
1965	3
1966	1
1967	6
1968	6
1969	7
1970	2
1971	4
1972	3
1973	2
1975	1
1978	1

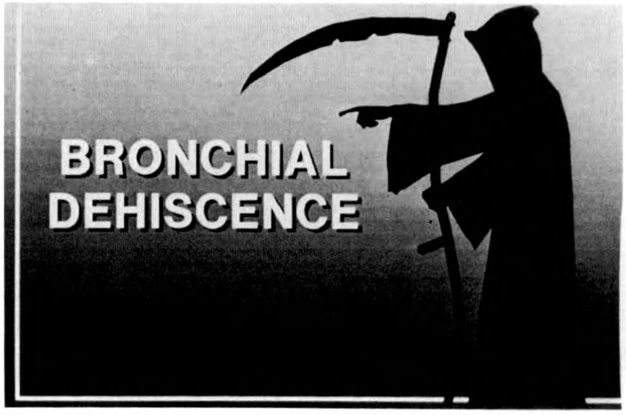


Fig 3. Bronchial dehiscence—the grim reaper of lung transplantation.

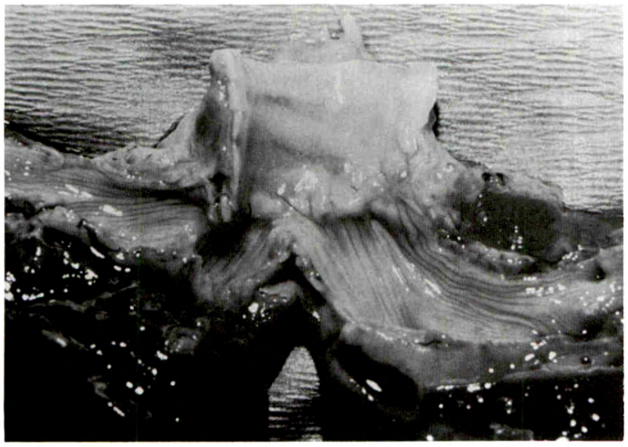


Fig 4. Bronchial anastomosis 3 weeks after lung reimplantation with no administration of immunosuppressive drugs. The wound is healed primarily, although some degree of circumferential narrowing is present.

He was left dependent on a ventilator, and both he and his family inquired as to the possibility of lung transplantation. One of my colleagues, Dr Bill Nelems, had studied with Dr Wildevuur in Holland and organized this transplantation. We were aware of the poor results in the past,

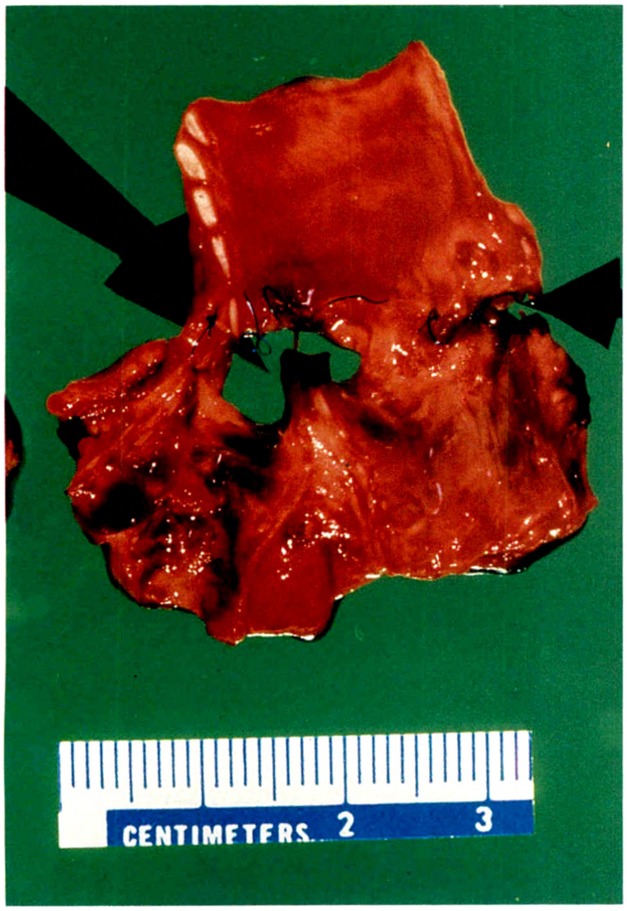


Fig 5. Bronchial anastomosis 2 weeks after lung reimplantation in a dog receiving prednisone and azathioprine.

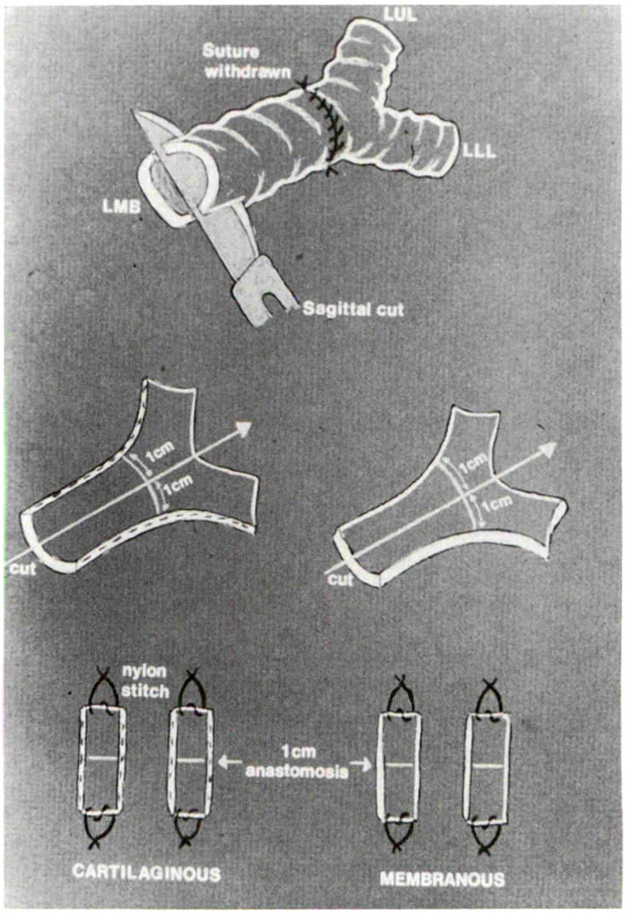


Fig 6. To evaluate breaking strength of a healing bronchial anastomotic wound, 1-cm-wide strips, perpendicular to the anastomosis, were prepared, and the amount of force necessary to disrupt the wound was measured. (LLL = left lower lobe; LMB = left main bronchus; LUL = left upper lobe.)

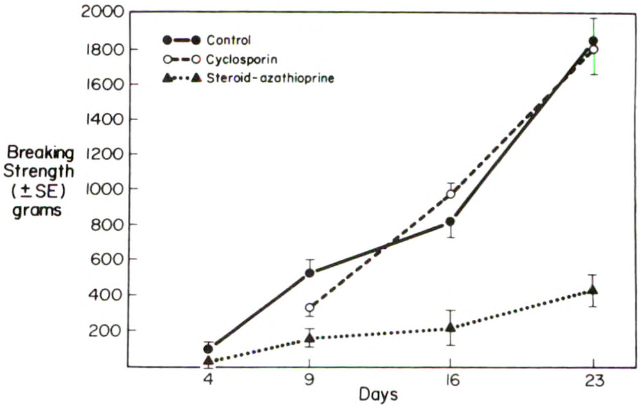


Fig 7. Breaking strength of healing wounds in animals receiving no immunosuppressive drugs (control), prednisone (2 mg/kg/day) plus azathioprine (1.5 mg/kg/day), or cyclosporin (20 mg/kg/day). The animals receiving prednisone and azathioprine showed marked inhibition of wound healing, whereas cyclosporin-treated animals were similar to controls.

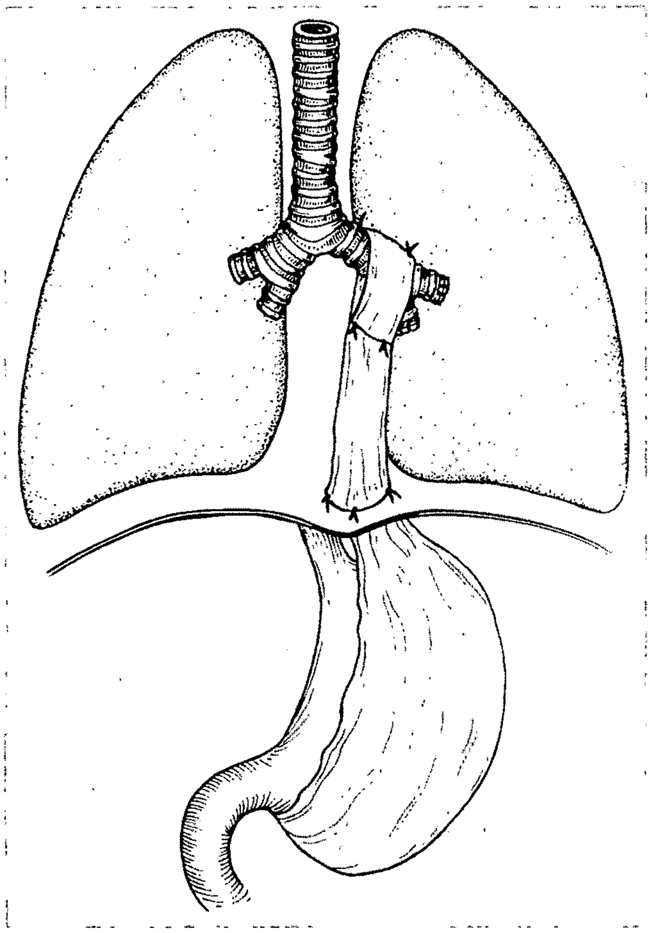


Fig 8. *The greater omentum is mobilized from the transverse colon and brought into the chest through a subxiphoid retrosternal tunnel. It is then brought posterior to the hilum of the lung and wrapped around the bronchial anastomosis.*

including the high incidence of early postoperative death. We thought we might have a better opportunity because of our experience with the use of a membrane oxygenator support system, which we had successfully applied to several patients suffering from acute respiratory failure. We believed that the availability of the membrane oxygenator system might improve our chances for success. By the time the patient underwent lung transplantation, his Pco_2 on maximum ventilatory assistance had risen to 130 mm Hg. He did require the use of the membrane oxygenator system before, during, and for two days after the procedure. Over the next 2 weeks the ventilatory systems could be discontinued and the patient became ambulatory (Fig 2). Unfortunately he died in the third postoperative week of disruption of the bronchial anastomosis.

A review of the world experience with human lung transplantation at the time revealed that approximately 38 lung or lobe transplantations had been attempted, with no long-term success, and with only 1 patient discharged alive from the hospital (Table 1). Of these 38 patients only 9 lived more than 2 weeks, the majority of whom died in the third week, as did our initial patient, of disruption of the bronchial anastomosis.

On the basis of these observations and this review, we believed that bronchial disruption was an important unsolved problem and decided to embark on no further lung transplantation until we had further understanding as to the cause of the problem and a means for its prevention (Fig 3). In the animal laboratory we began investigations into factors affecting bronchial healing after lung transplantation. We considered at least three factors that might relate to the problem. The first was rejection, which many considered the most likely factor responsible for the repeated failure of the bronchial anastomosis to heal. Ischemia was another potential factor that needed to be considered. The lung is unique among organ transplants in that its systemic, arterial supply is not reattached at the time of transplantation. With other organ transplants the systemic vessels are reattached, but the fine network of bronchial vessels is not easily amenable to reattachment at the time of lung transplantation. Such reattachment has been accomplished experimentally [3], and the restoration of bronchial circulation was demonstrated to improve bronchial healing.

A third factor we considered was the use of immunosuppressive agents, namely prednisone and azathioprine, that might prejudice healing of the bronchial anastomosis.

To begin the investigations we did a series of experiments with lung reimplantation in the dog, namely, the severing and reattachment of the left lung. With this model, of course, factors associated with rejection are eliminated, but any factors relating to the severing and

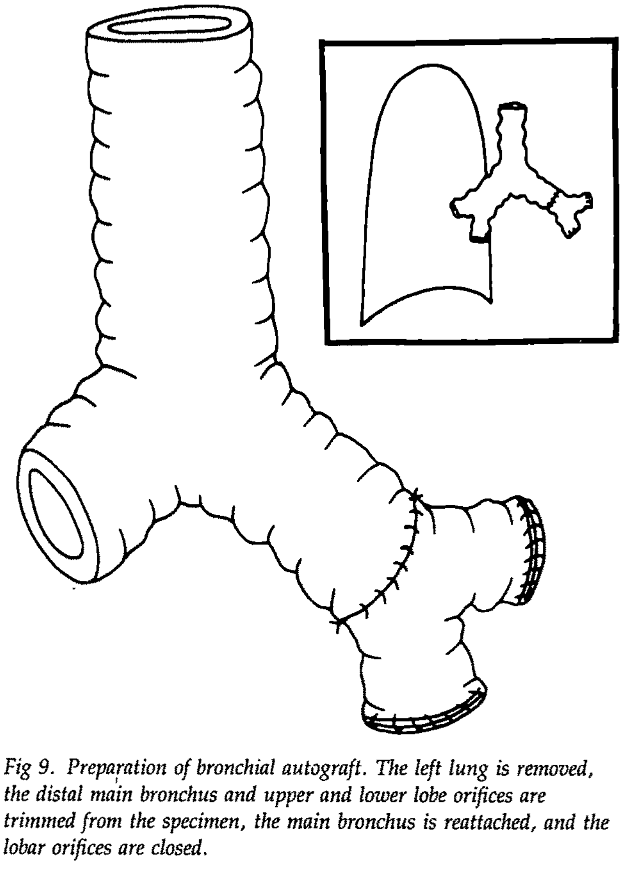


Fig 9. *Preparation of bronchial autograft. The left lung is removed, the distal main bronchus and upper and lower lobe orifices are trimmed from the specimen, the main bronchus is reattached, and the lobar orifices are closed.*

reattachment of a lung are incorporated. Half the animals received no immunosuppressive drugs, whereas the other half were treated with the same doses of immunosuppressive drugs as would be given had a transplantation been performed.

Animals receiving no immunosuppressive drugs showed, in general, primary healing of the bronchial anastomosis, although a moderate degree of narrowing often occurred at the anastomosis (Fig 4). On the other hand, animals receiving prednisone and azathioprine showed the same type of bronchial complications as had been observed in human transplants, namely, disruption of the bronchial anastomosis and poor mucosal healing just distal to the anastomosis [4] (Fig 5).

To study bronchial healing a bit more objectively we killed animals at various intervals after lung reimplantation, excised the length of bronchus containing the anastomosis, cut this into 1-cm-wide vertical strips, and studied the breaking strength of the healing bronchial anastomotic wound (Fig 6). In the animals receiving no immunosuppressive drugs the breaking strength of the anastomosis increased with time; over the first 3 weeks there was a continuous increase in the breaking strength. In the animals receiving azathioprine and prednisone, however, there was marked inhibition of wound healing as evidenced by measurements of the breaking strength.

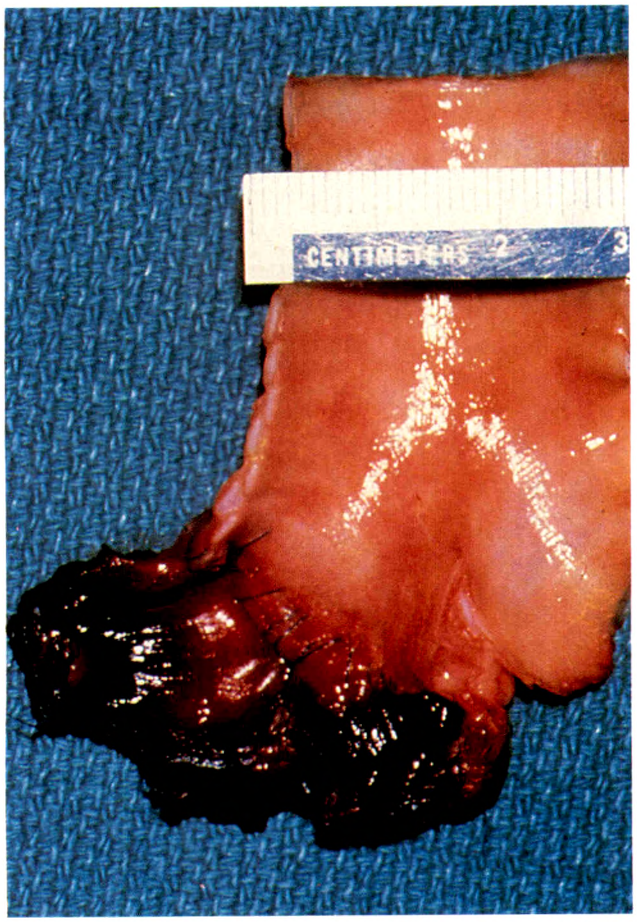


Fig 10. Bronchial autograft prepared as in Figure 9, shown four days after operation with extensive gangrenous necrosis. (From [7]. Reprinted with the permission of the C.V. Mosby Company.)

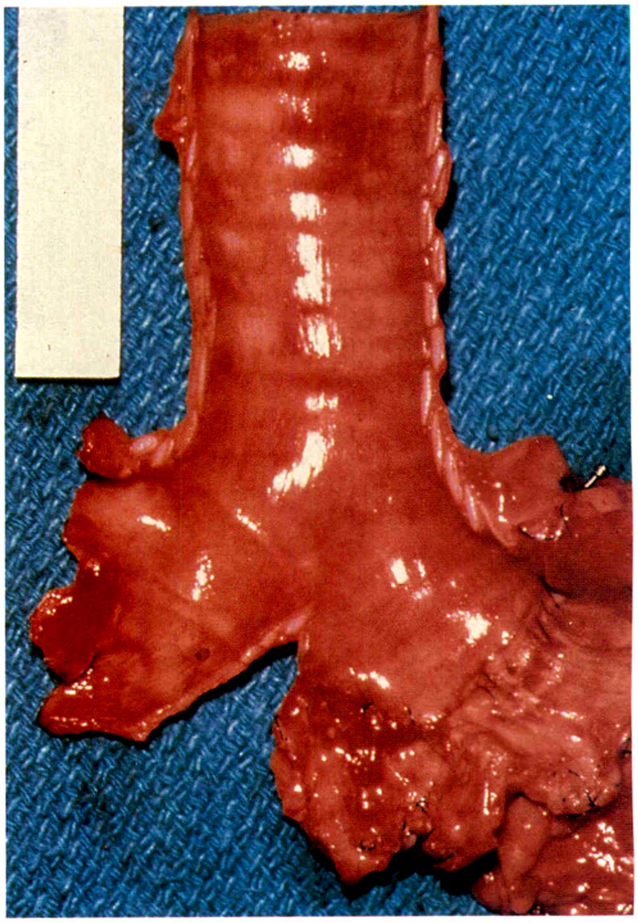


Fig 11. Bronchial autograft (lower right) 3 weeks after its preparation. The graft was wrapped with the omentum at the time of its reconnection to the left main bronchus. The bronchial anastomosis healed primarily and histology revealed normal mucosa and cartilage in the graft.

At about this time a new drug, cyclosporin, was becoming available in small amounts for research purposes. We were able to secure some of this and repeated the same experiments using cyclosporin rather than azathioprine and prednisone [5]. We found that with cyclosporin, there was no inhibition of wound healing and the breaking strength of the anastomotic site was the same as in the untreated animals (Fig 7). In subsequent studies we evaluated azathioprine and prednisone separately and found, as might be expected, that the prednisone was solely responsible for inhibition of healing of the bronchial anastomotic wound.

At this point we had learned several things; namely, that routine use of prednisone after lung transplantation seriously interfered with bronchial anastomotic healing and that the use of cyclosporin instead of prednisone in the early postoperative period did not pose any problems.

As noted earlier, the bronchial anastomosis healed with some degree of narrowing in most animals, even in the absence of immunosuppressive drugs. This narrowing was distal to the suture line, and we attributed it to the effects of ischemia. To address this problem we used an old surgeons' trick, the omentum. This marvelous, mag-

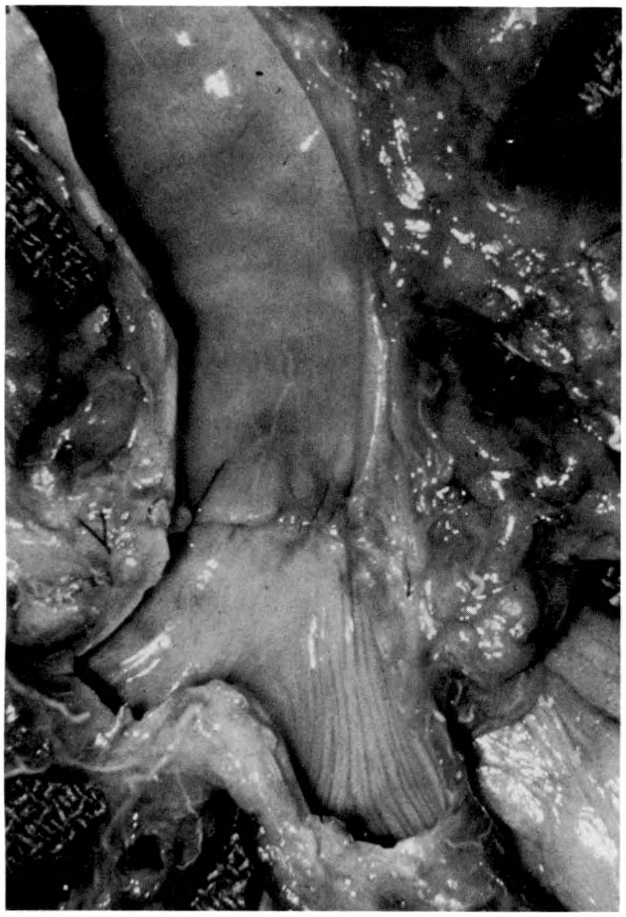


Fig 12. Canine bronchial anastomosis 3 months after lung transplantation. The bronchus was wrapped with omentum at the time of transplantation. Initial immunosuppression consisted of cyclosporin and azathioprine, with prednisone added at 3 weeks.

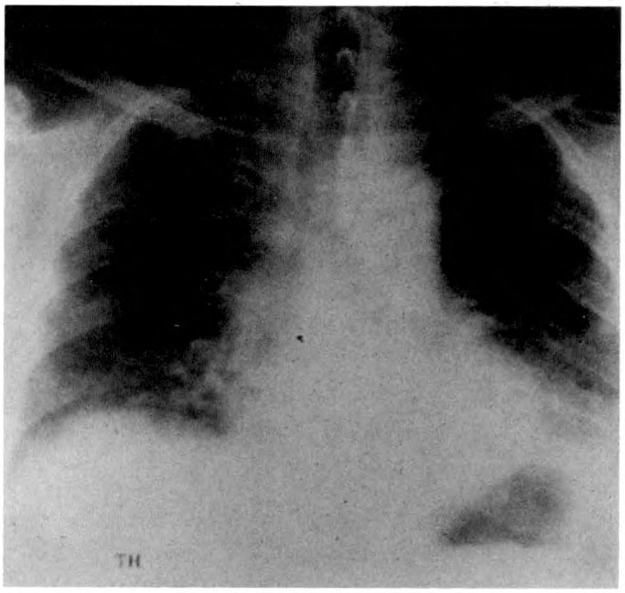


Fig 13. Preoperative chest roentgenogram of a 58-year-old man with idiopathic pulmonary fibrosis. The lung fields are contracted. Reprinted by permission of the New England Journal of Medicine *(1986;314:1140–5).*

ical organ has long been known by surgeons for its ability to rapidly bring in new blood supply. Because of its long vascular pedicle it has been brought to many areas of the body to improve healing and restore circulation. In this regard I first observed its use by Dr Grillo when I was a resident. He used it to wrap around the trachea when creating a mediastinal tracheotomy.

We decided to bring the omentum into the chest and wrap it around the bronchial anastomosis at the time of lung transplantation (Fig 8). We did a series of lung transplantations, killing animals at various intervals and injecting the omental vessels to determine how rapidly collateral circulation between the omentum and the bronchial circulation would occur. We found that in each and every case collateral circulation between omental vessels and bronchial vessels distal to the anastomosis had been accomplished by four days. It was known that it normally takes 2 to 3 weeks for bronchial circulation to be restored by means of vascular growth across the healing bronchial anastomosis after lung transplantation [7].

To evaluate the capability of the omentum to generate collateral circulation to the airway, we performed the following experiment. The left lung of the dog was removed and the left main bronchus and a portion of the left upper and lower lobe bronchi were excised from the specimen. The lobar orifices were closed and the left bronchus was reattached to the proximal left main bronchus from which it had been severed (Fig 9). The purpose of this experiment was to deprive the grafted bronchial segment of any collateral circulation coming up the bronchial vessels in retrograde fashion from the pulmonary circulation. With this model the bronchial stump is totally ischemic.

Not surprisingly, each and every animal died within five days of gangrenous necrosis of the bronchial stump with formation of bronchal pleural fistula and empyema (Fig 10). On the other hand, when the experiment was repeated using the omentum to wrap around the implanted bronchial stump, all animals survived. When these animals were killed at 3 weeks, the bronchial autograft was perfectly viable, complete with its mucosa, cartilage, and a demonstrable circulation [7] (Fig 11).

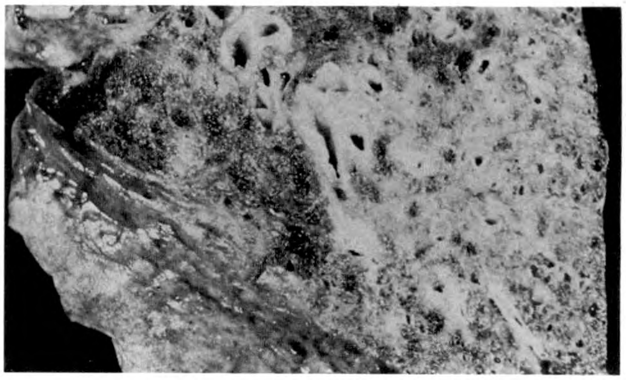


Fig 14. Cut surface of lung removed for pulmonary fibrosis showing dense scarring and honeycombing.

We next performed a series of lung transplantations in dogs using the omentum to protect and nourish the bronchus and administering cyclosporin rather than prednisone for the initial few weeks, after which prednisone was added to the immunosuppressive regimen. These animals were killed at 3 months and in general showed excellent bronchial anastomotic healing (Fig 12). Finally, after these experiments we went to the autopsy room and performed a series of lung transplantations in cadavers to practice the technical aspects of the procedure. We then felt ready to embark on a cautious program of human lung transplantation.

From our primary review of the literature it was apparent that most clinical lung transplantations had been performed under relatively adverse circumstances, often on ventilator-dependent, debilitated, infected patients with multisystem problems in whom transplantation was utilized as a last-ditch effort. We believed that, at least initially, we should limit the procedure to patients with progressive end-stage pulmonary disease with limited life expectancy who were not yet hospital-dependent or ventilator-dependent. We believed that patients with end-stage pulmonary fibrosis represented the ideal candidates. Such patients generally do not have chronic pulmonary sepsis, so the remaining lung would not jeopardize the new lung. The reduced compliance of the native, fibrotic lung would help ensure that ventilation goes preferentially to the transplanted lung. The increased vascular resistance in the diseased lung would help ensure that most of the blood flow would likewise be diverted to the transplanted lung.

In 1983 a 58-year-old patient heard about our transplantation program and inquired as to the possibility of a lung transplantation. At the time he was on oxygen 12 hours a day, and although he was disabled we believed he was not yet at the end of the line, and thus the great risks of transplantation were not yet justified. Six months later, however, the situation had changed. He was on oxygen 24 hours a day and had shown progressive disability such that, in our opinion, life expectancy was only a matter of months (Fig 13).

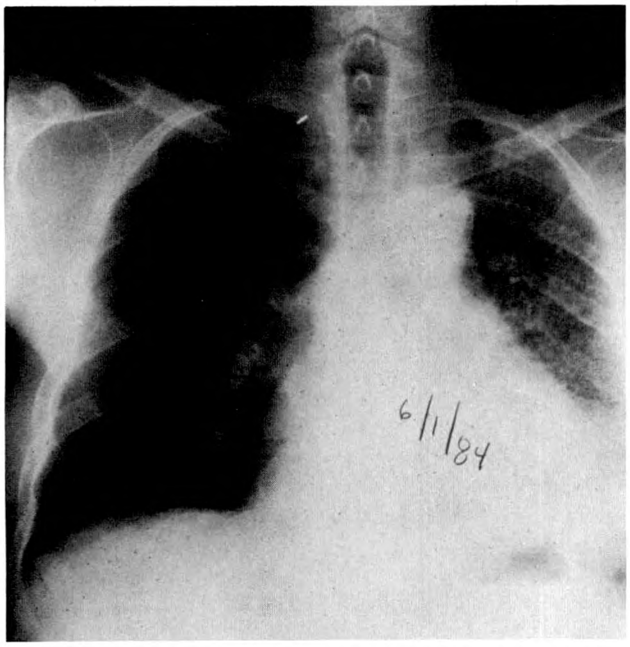


Fig 15. Chest roentgenogram 3 months after right lung transplantation for idiopathic pulmonary fibrosis. The chest configuration on the transplanted side shows a more normal configuration and a clear lung field.

Fig 16. Our first successful lung transplant recipient shown several months after right lung transplantation. The patient continues to enjoy good health 5 years after his transplantation.

He underwent a right lung transplantation on November 7, 1983, was discharged from the hospital in 6 weeks, and returned to work in 3 months (Figs 14 and 15). He has continued to work and to enjoy good health ever since; it is now 5 years after his transplantation (Fig 16).

The procedure that we use for lung transplantation varies little from the technique used in animals and humans over the years [8]. The patient initially is placed in the supine position, and a small upper midline incision is used for mobilization of the omentum (Fig 17). In the future, we plan to do this with the patient in the thoracotomy position. It is generally easy to obtain sufficient length with little more than detachment of the omentum from the transverse colon. Once the omentum has been mobilized, a retrosternal tunnel is made immediately behind the xiphisternum and the apex of the omentum is

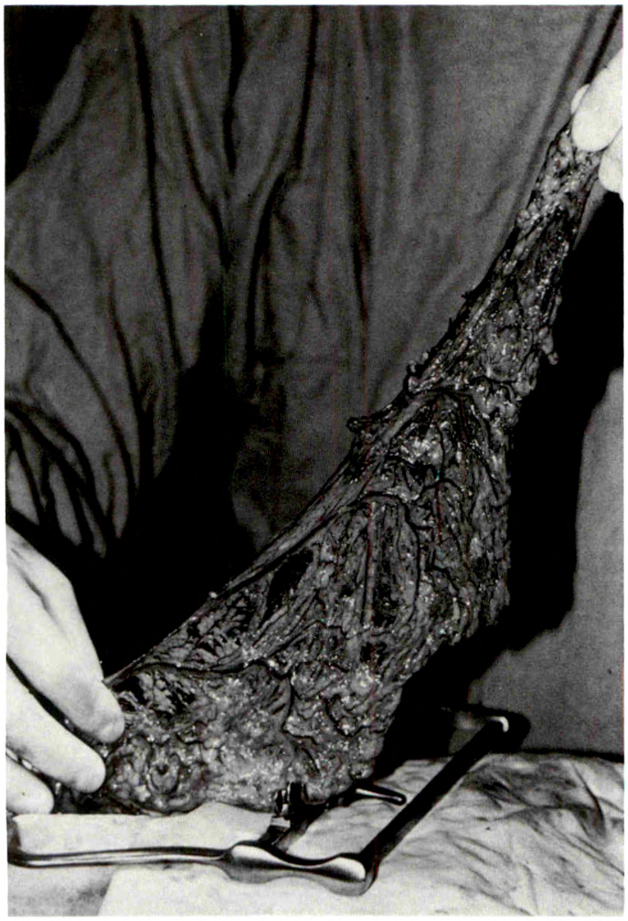


Fig 17. *Mobilizing the greater omentum from the transverse colon usually provides sufficient length to reach the bronchial anastomosis.*

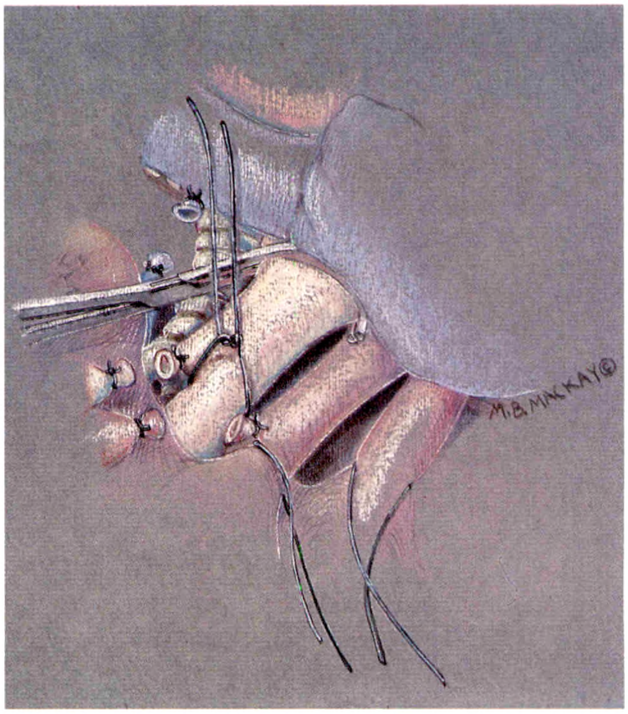


Fig 18. *Illustration of right lung removal for transplantation. When the chest is first entered the pulmonary artery is temporarily occluded near its origin to determine if the recipient will tolerate one-lung anesthesia. The pulmonary artery is subsequently divided distal to its first branch to provide additional length. The pulmonary veins are initially divided close to the hilum of the lung.*

placed in this tunnel before the abdominal incision is closed. The recipient is then turned into the lateral thoracotomy position. We find the left lung transplantation technically somewhat simpler, although either side can be utilized with similar results. Once the chest has been entered the pulmonary artery is isolated intrapericardially and temporarily clamped to determine whether or not the recipient will require the use of cardiopulmonary bypass during extraction and replacement of the lung (Fig 18). To date this has been necessary in 25% of patients. If clamping of the pulmonary artery is poorly tolerated, the clamp is removed and the femoral vessels on the side of thoracotomy are prepared for subsequent cannulation.

The lung is extracted by division of the pulmonary veins close to the lung, division of the pulmonary artery distal to its first branch, and division of the bronchus just proximal to the upper lobe takeoff.

Even when bypass is temporarily required, complete mobilization of the lung is performed before bypass, so that hemostasis can be achieved before heparin administration. After removal of the native lung, the pericardium is completely opened around the pulmonary veins and a vascular clamp is placed on the left atrium as centrally as possible without impinging on the contralateral pulmonary veins. On the right side it may be necessary to dissect into the intraatrial groove to mobilize sufficient left atrium for satisfactory clamping of the atrium. Once the atrial clamp has been placed, the previously placed ligatures on the pulmonary venous stumps are removed and the bridge between the pulmonary veins is divided to provide a suitable atrial cuff (Fig 19).

The donor lung is placed in the chest (Fig 20) and the

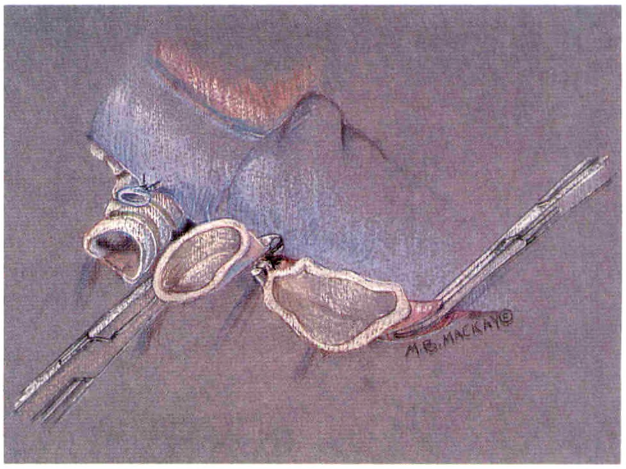


Fig 19. *After removal of the lung, the pericardium is opened completely around the pulmonary veins, and a vascular clamp is placed on the left atrium. An incision is made joining the stumps of the two pulmonary veins to create a generous cuff of left atrium.*

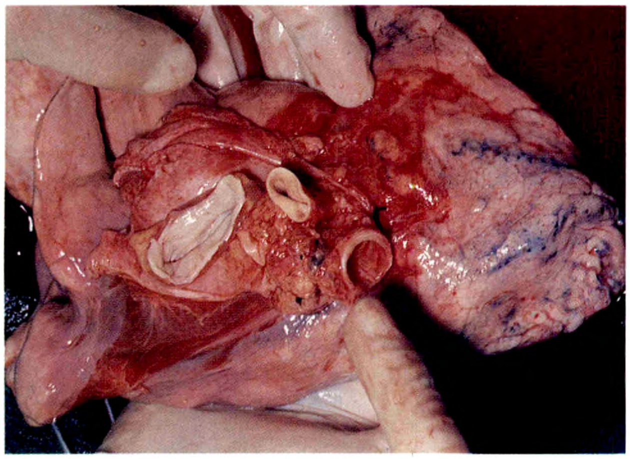


Fig 20. Right donor lung showing preparation of bronchus, pulmonary artery, and left atrial cuff. The bronchus is divided two rings above the right upper lobe orifice.

atrial anastomosis is performed using a running 3-0 polypropylene suture.

The donor and the recipient pulmonary arteries are then trimmed if necessary and proper orientation is determined. The previously ligated first branch of the recipient pulmonary artery and the first branch of the donor pulmonary artery can be lined up to ensure that no rotation occurs. The arterial anastomosis is performed with a continuous 5-0 polypropylene suture, interrupted at two points (Fig 21). Upon completion of the arterial anastomosis, the suture is left untied to allow subsequent flushing and back-bleeding after completion of the bronchial anastomosis.

We initially performed the bronchial anastomosis after restoration of flow to the transplanted lung to minimize ischemic time. This, however, required ventilation of the lung through the open bronchus, which proved complicated and unnecessary. Therefore we now complete the bronchial anastomosis first, using interrupted 4-0 absorbable sutures. The atrial clamp is removed, the lung is gently inflated, and, after back-bleeding from the pulmonary artery suture line has been observed or after three to five minutes if such back-bleeding has not occurred, the pulmonary artery clamp is removed and the arterial suture line is tied. The omentum is retrieved from its retrosternal position, brought inferior and posterior to the hilum of the lung, and passed completely around the bronchus so as to encircle it (Fig 22). The omentum is tacked to itself to avoid subsequent displacement.

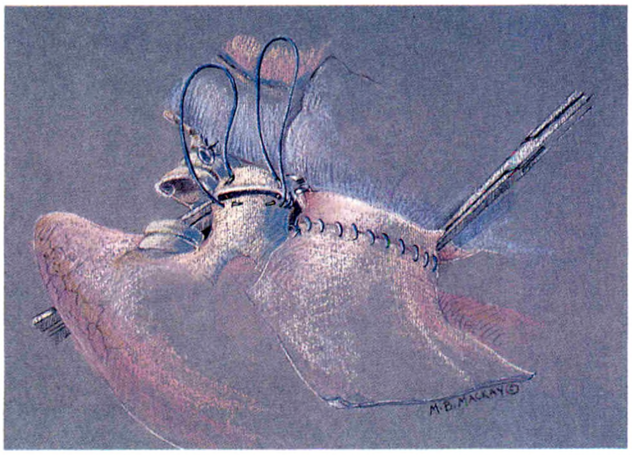


Fig 21. The right atrial anastomosis is performed initially, followed by the pulmonary arterial anastomosis. The pulmonary arterial suture is not tied until the bronchial anastomosis is subsequently completed and the left atrial clamp has been removed to allow back-bleeding.

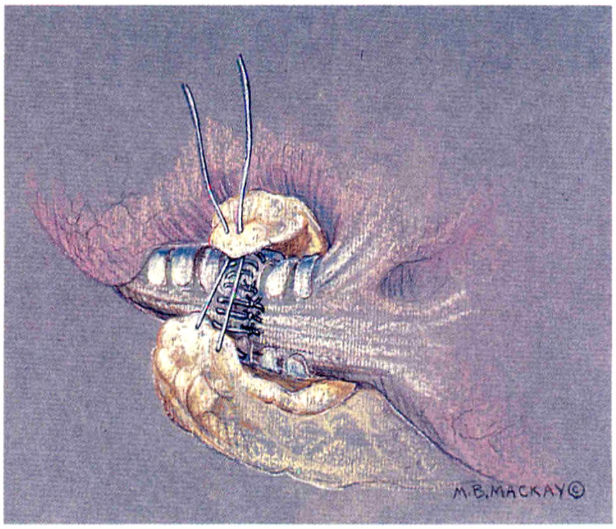


Fig 22. After completion of the bronchial anastomosis the omentum is brought inferior and posterior to the hilum of the lung, passed completely around the bronchus, and sutured to itself to prevent slippage.

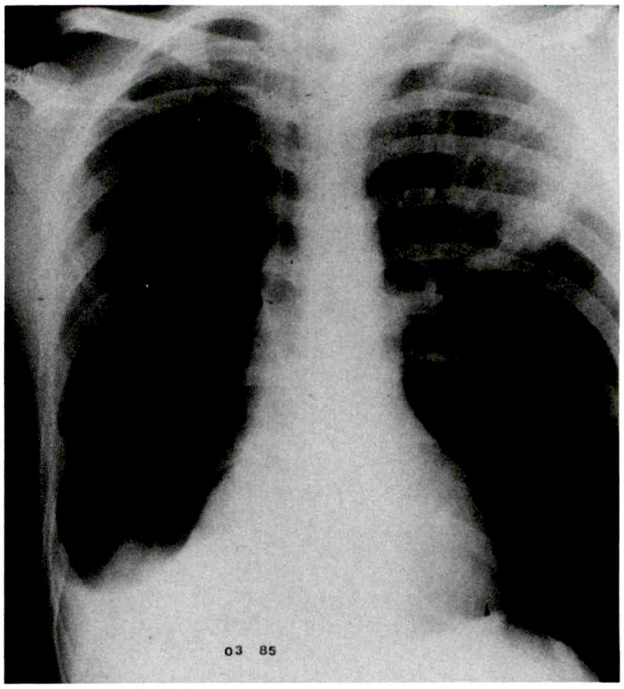


Fig 23. Chest roentgenogram of a 28-year-old man with congenital agammaglobulinemia and resultant chronic bronchiectasis and emphysema.

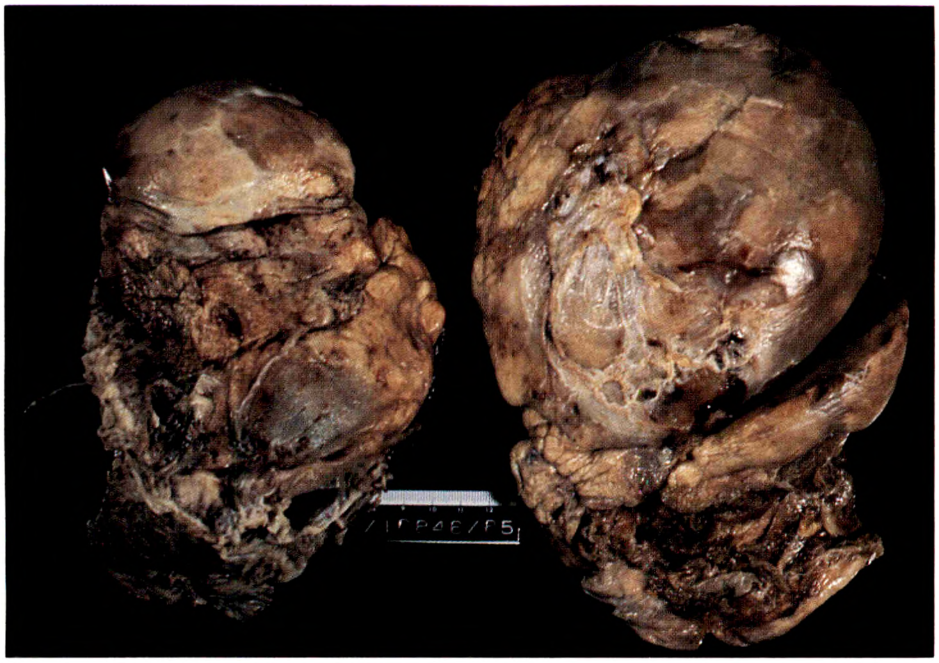


Fig 24. *Excised lungs from patient with congenital agammaglobulinemia who underwent combined lung-heart transplant procedure.*

From the period of November 1983 to June 1988, 16 lung transplantations were performed at the Toronto General Hospital. No patient died as a result of bronchial complications. There were 4 in-hospital deaths and 12 hospital survivors at risk for development of delayed complications. Of these 12, 2 patients developed late bronchial stenosis. Each of these was managed by dilatation and subsequent endoscopic implantation of a silicone stent.

Pulmonary sepsis, emphysema, and right ventricular failure have all been considered contraindications to single-lung transplantation. We have believed that single-lung transplantation is contraindicated in the presence of bilateral pulmonary sepsis such as cystic fibrosis because infection in the remaining lung would jeopardize the new lung, and the patient in general. With obstructive lung disease such as emphysema, we have been concerned that unilateral transplantation might lead to overinflation of the contralateral lung with displacement of the mediastinum toward the transplanted lung. We were impressed with the early results obtained at Stanford University with the combined heart-lung transplantation, previously utilized by them for patients with a combina-

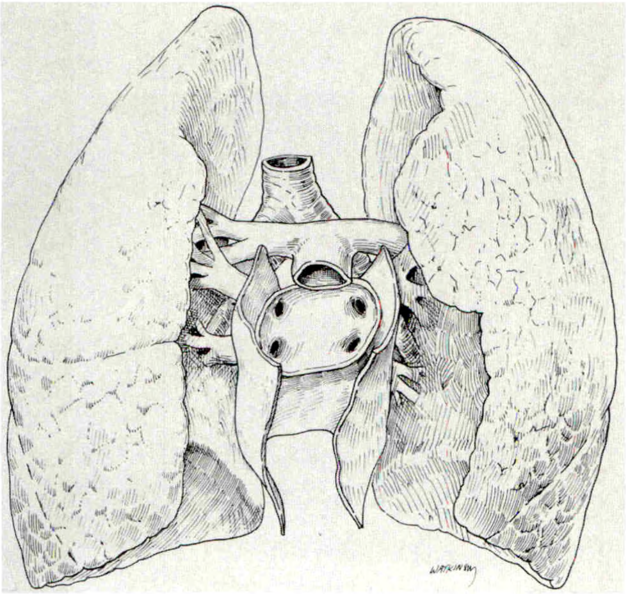


Fig 25. *Schematic of double-lung graft. The two lungs remain joined by the trachea, the common pulmonary artery, and the back wall of the left atrium containing the four pulmonary veins.*

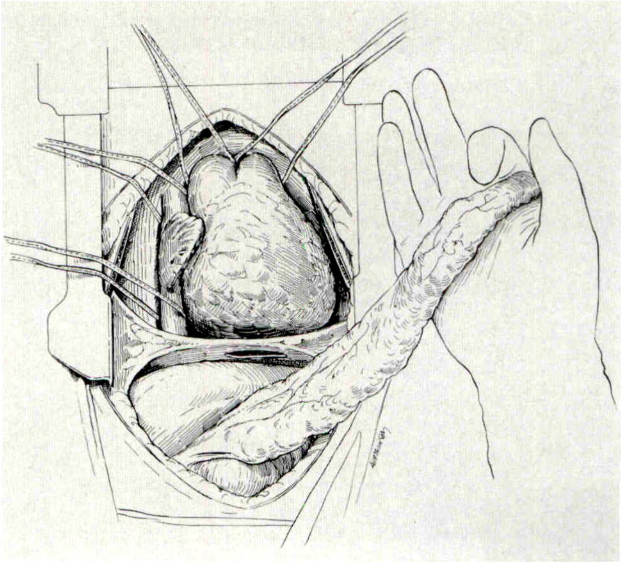


Fig 26. *For double-lung transplantation, the sternotomy incision is extended onto the upper abdomen for mobilization of the omentum. A small fenestration is created in the diaphragm for subsequent passage of the omentum behind the heart and into the superior mediastinum.*

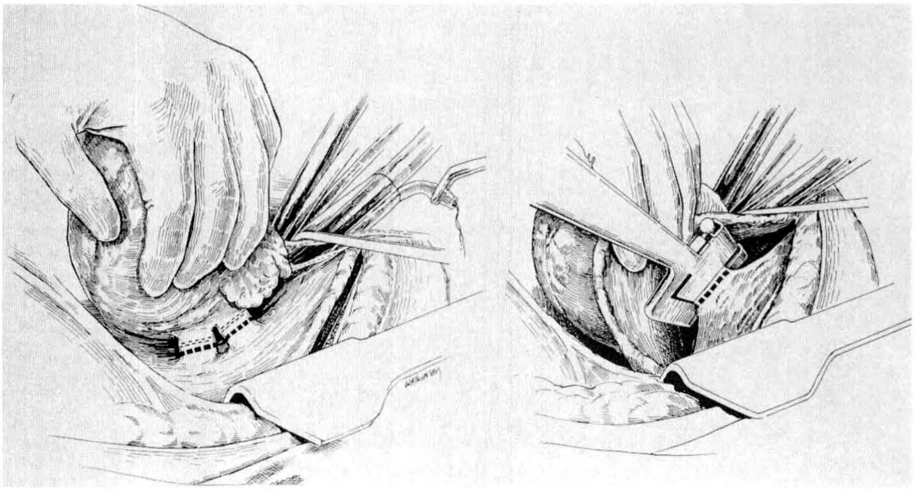


Fig 27. After institution of cardiopulmonary bypass the left lung is removed. The pulmonary veins are stapled intrapericardially (as shown on the left) and the left pulmonary artery is stapled and divided either extrapericardially (as shown on the right) or intrapericardially.

tion of right heart failure and increased pulmonary vascular resistance, especially primary pulmonary hypertension and Eisenmenger's syndrome. We decided to employ this procedure for patients with end-stage lung disease. From this experience we concluded that the majority of patients requiring transplantation for end-stage lung disease have adequate or recoverable right heart function and, theoretically at least, do not require replacement of the heart as well.

One such patient was a 28-year-old man with congenital agammaglobulinemia, whose immune deficiency led to repeated pulmonary infections with destruction of his lungs (Fig 23). He underwent combined heart-lung transplantation with excision of the scarred, infected lung and removal of a normal heart (Fig 24). It was this case more than any other that convinced us of a need for simultaneous replacement of both lungs in those patients with end-stage lung disease who might not be suitable for unilateral lung transplantation. We had thus defined another clinical problem and the whole cycle of investigation was repeated including development of an animal model, experimentation with different techniques, modification of the animal techniques for human use using cadaver dissections, and application of the procedure in humans. We were especially concerned about the blood supply to the trachea, as the tracheal anastomosis is that much further away from the hilum of the lung and retrograde bronchial circulation is likely to be even more inadequate during the early posttransplantation period. With the combined heart-lung transplantation, small branches of the coronary circulation through the pericardium are thought to supply the subcarinal bronchial vessels directly and thus maintain the tracheal circulation.

Initial experiments were conducted in dogs, but as dogs are unable to adequately breathe after bilateral pulmonary denervation, long-term experiments required a primate model. Experiments were conducted using profound hyperthermic arrest in a small primate species. The model proved difficult to use, but sufficient progress was obtained to suggest that simultaneous double-lung trans-

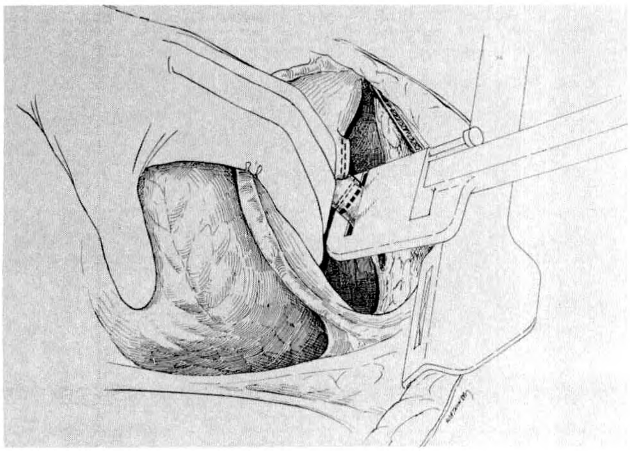


Fig 28. The left main bronchus is divided between staple lines to avoid contamination. The left lung is then removed from the chest.

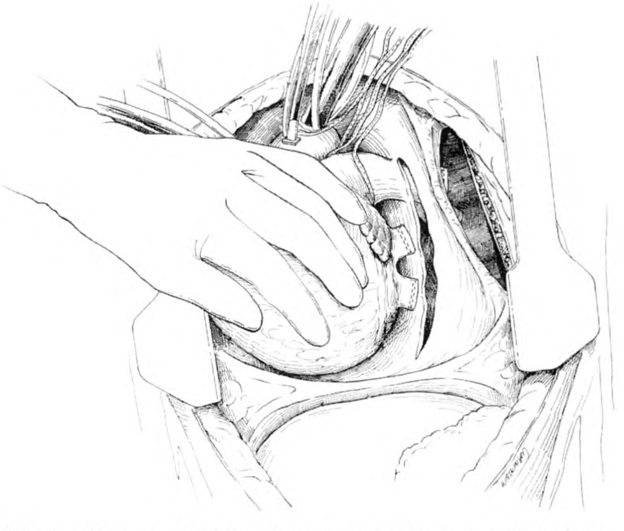


Fig 29. After removal of the left lung, the pericardium is opened posterior to the phrenic nerve, from the diaphragm to the aortic arch, to create a pleuropericardial window for later passage of the left lung into the pleural space.

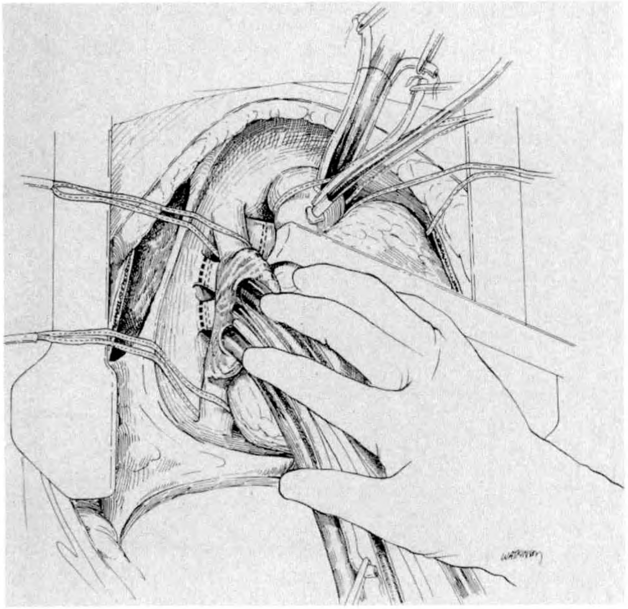


Fig 30. The right pulmonary artery is stapled in the mediastinum between the superior vena cava and the aorta. It is subsequently divided lateral to the pericardium. The pulmonary veins are stapled within the pericardium and divided just lateral to the staple line.

plantation was feasible [9]. The technique we have employed [10] utilizes a median sternotomy, bilateral pneumonectomy, and implantation of the double-lung block with three anastomoses: the trachea, the common pulmonary artery, and a cuff of donor left atrium containing the pulmonary veins (Fig 25). The tracheal anastomosis is wrapped with omentum as is the bronchial anastomosis in single-lung transplantation. In addition to allowing the recipient to retain his or her own heart, a major advantage of the double-lung procedure (as with the single-lung procedure) is the ability to utilize suitable lungs from heart transplant donors, which would otherwise be discarded. This greatly increases the number of potential transplants available for patients with end-stage lung diseases.

The procedure is similar to the combined heart-lung

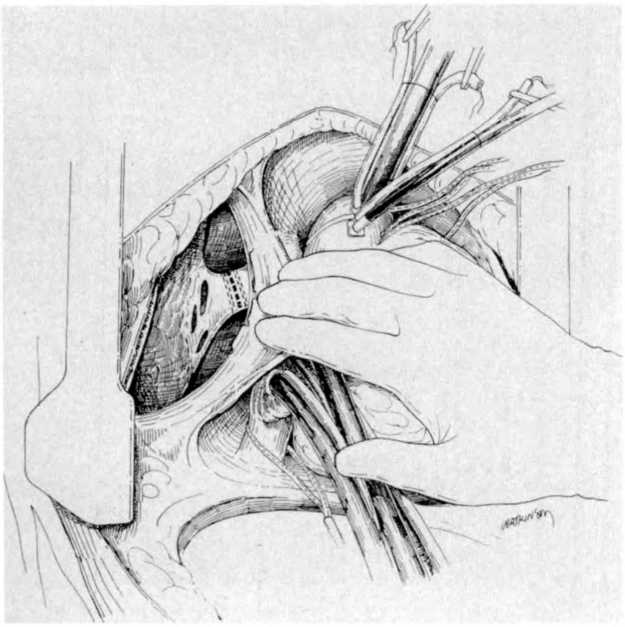


Fig 31. The right main bronchus is divided between staple lines, after which the right lung is removed.

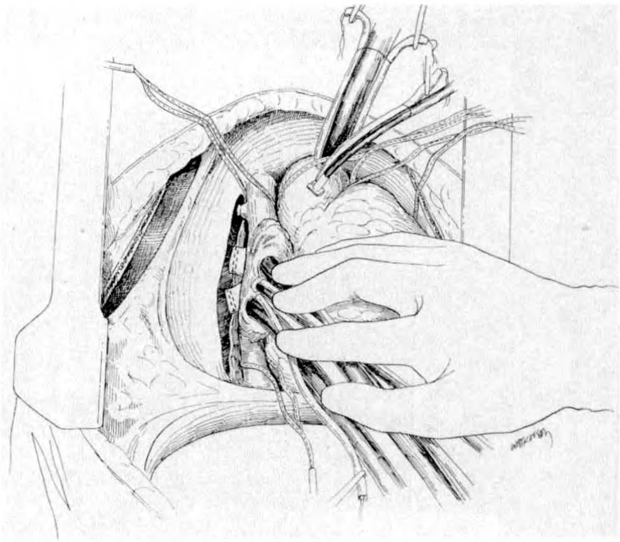


Fig 32. After removal of the right lung, a pleuropericardial window is created posterior to the phrenic nerve from the diaphragm to the azygous vein, which can be divided to allow upward extension of the pericardial window.

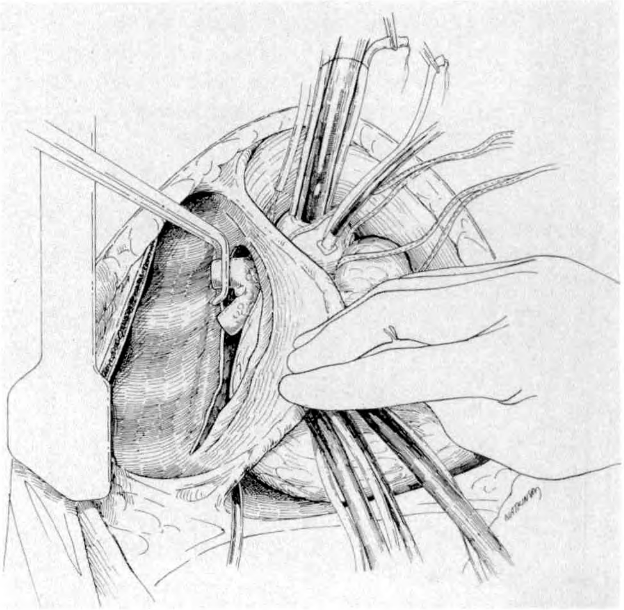


Fig 33. The right bronchial stump is grasped with a clamp and pulled into the right pleural space. Using cautery dissection, the right and left bronchi and the carina are dissected free. The clamp is then removed and the airway retracts back into the mediastinum, where it will subsequently be divided just above the carina for the tracheal anastomosis.

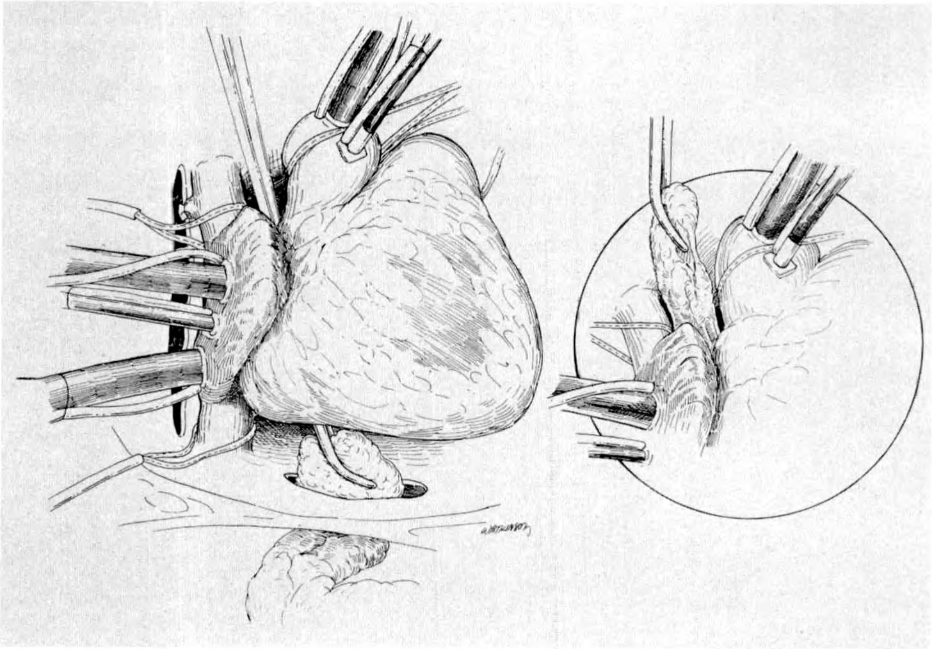


Fig 34. The previously mobilized omentum is withdrawn through the diaphragmatic fenestration and behind the heart into the superior mediastinum before insertion of the double-lung block.

transplantation on which it was based. The omentum is mobilized and as much interthoracic dissection performed as possible before administration of heparin for bypass (Fig 26). The left pulmonary veins and pulmonary artery are stapled (Fig 27) and the left lung is excised, dividing the left main bronchus between staple lines (Fig 28). A pericardial window is made posterior to the phrenic nerve for later passage of the lung into the pleural space (Fig 29). The right lung is similarly excised, dividing the veins, the artery (Fig 30), and the bronchus (Fig 31), and creating a pleuropericardial window posterior to the phrenic nerve (Fig 32). The distal trachea and both bronchial stumps are then dissected free (Fig 33). The previously mobilized omentum is passed through a fenestration in the diaphragm, behind the heart, and onto the superior mediastinum (Fig 34). The recipient heart is then elevated, the donor specimen is placed behind the heart, and each lung is directed through a pleural pericardial window into the respective pleural space (Fig 35). The donor trachea is pulled up into the superior mediastinum between the aortic arch and the superior vena cava. The donor and the recipient tracheas are respectively transsected just above the carina and an end-to-end anastomosis is performed (Fig 36). Under cardioplegic arrest, the recipient heart is elevated, an incision is made in the back of the left atrium (Fig 37), and an anastomosis is performed between the donor atrial cuff and the back of the recipient left atrium (Fig 38). The recipient heart is then returned to its normal position. The common pulmonary artery of the recipient is transsected proximal to its bifurcation and an anasto-

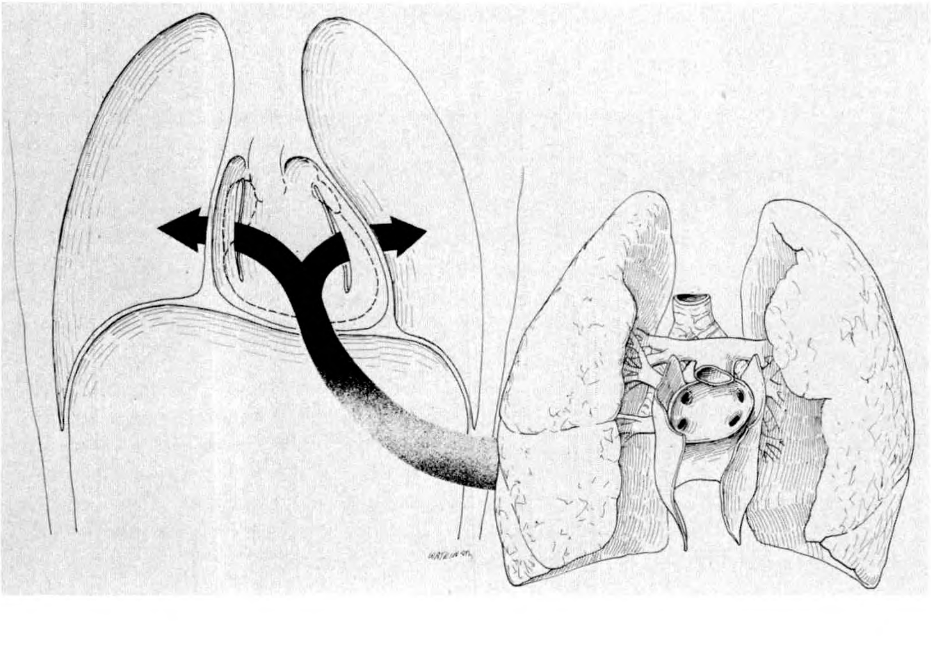


Fig 35. With the apex of the heart elevated, the double-lung block is inserted into the posterior mediastinum and each lung is directed into its respective pleural space through the previously created pleuropericardial windows. An umbilical tape (not shown here) attached to the trachea facilitates withdrawal of the trachea into the superior mediastinum after the lungs have been properly positioned.

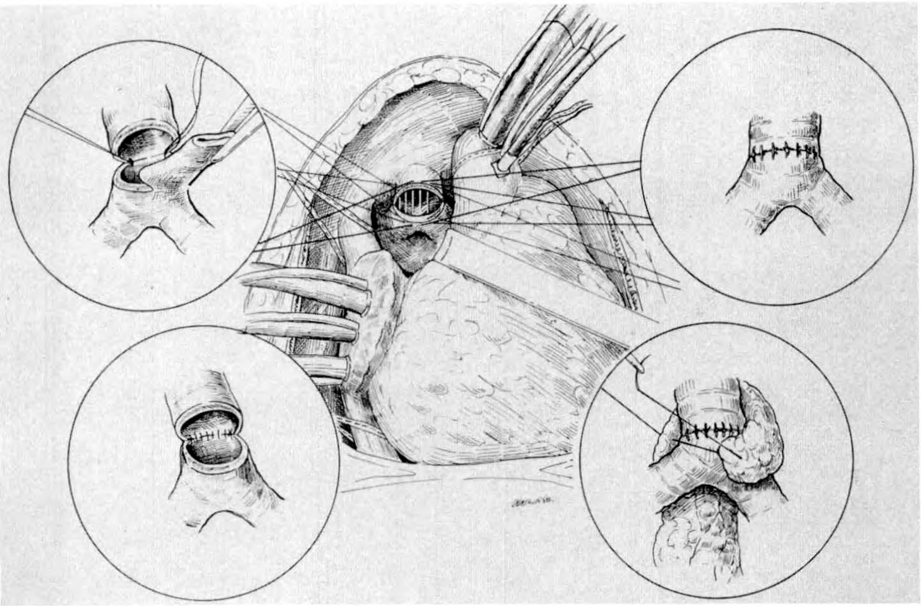


Fig 36. The recipient trachea is divided just above the carina with removal of the carina and left and right bronchial stumps. The donor trachea is divided just above the carina (upper left) and the posterior portion of the tracheal anastomosis is performed with a running monofilament suture (lower left). The cartilaginous portion of the tracheal anastomosis is performed with interrupted absorbable sutures (upper right), after which the omentum is securely wrapped completely around the tracheal anastomosis (lower right).

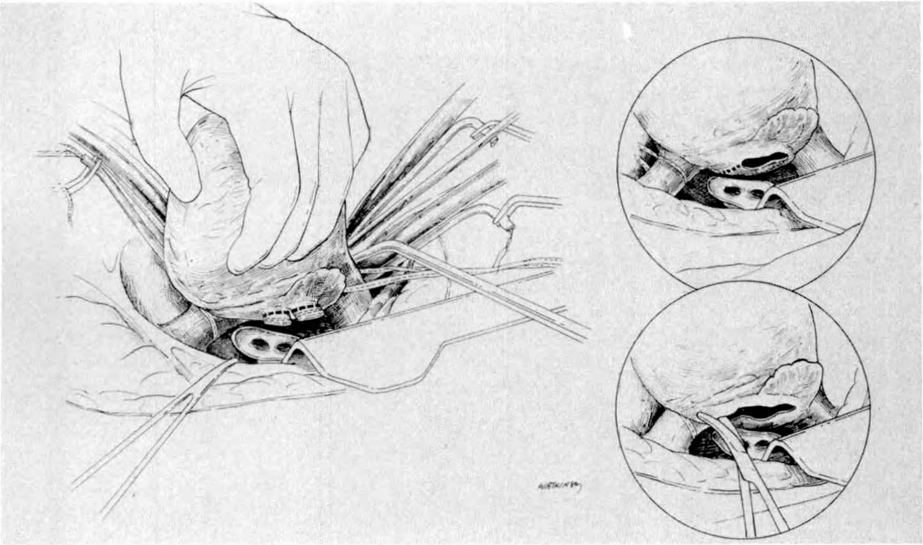


Fig 37. After the tracheal anastomosis, the heart is arrested with infusion of cold cardioplegic solution. At this point the tourniquets surrounding the caval cannulas can be tightened. With the apex of the heart elevated, an opening is created in the back of the left atrium. Initially the stumps of the left pulmonary veins are excised (upper right), and the opening in the atrium is extended by incision of the back wall of the atrium transversely (lower right). Further enlargement can be obtained by incision into the atrial appendage if necessary.

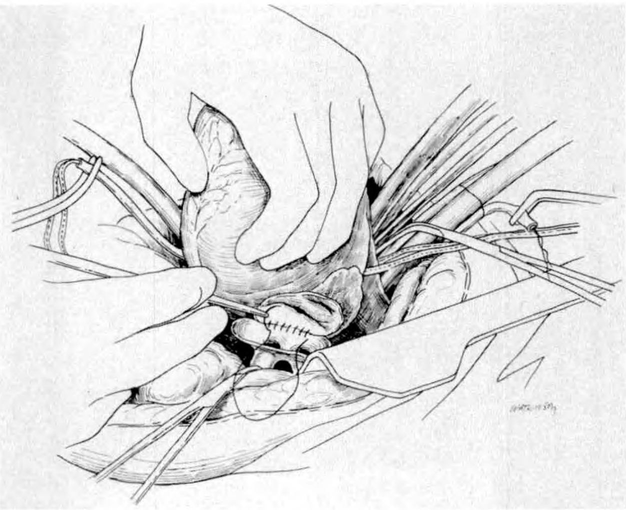


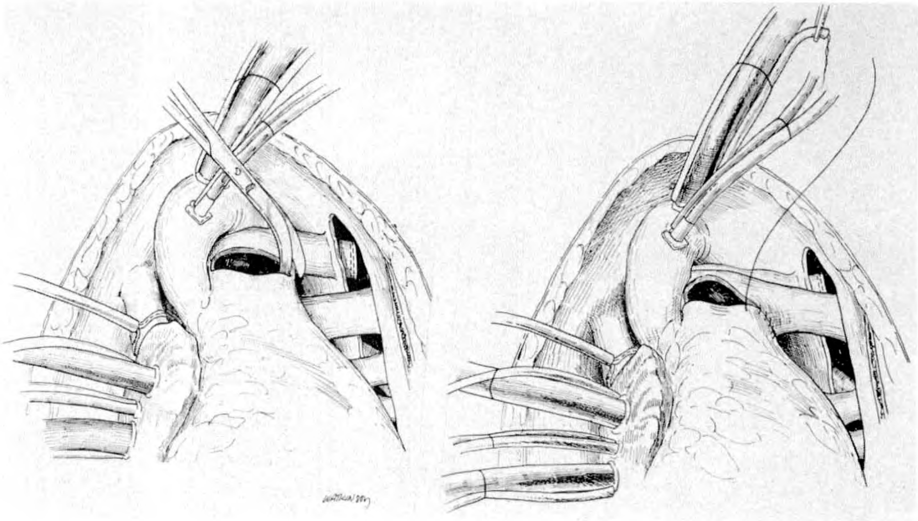
Fig 38. The donor atrial cuff is anastomosed to the opening in the back of the recipient left atrium using a running monofilament suture.

mosis is constructed in end-to-end fashion with the donor pulmonary artery (Fig 39).

The initial recipient, a 34-year-old woman with end-stage emphysema secondary to α_1-antitrypsin deficiency, remains in excellent health 2 years after the transplantation (Fig 40). The configuration of her chest returned to normal very quickly (Fig 41). However, the patient did develop a delayed stenosis of the proximal left main bronchus several months after the transplantation. This was treated with dilatation and insertion of a Y-shaped silicone prosthesis placed at the carina and extending into each main bronchus.

Although 8 of the first 9 double-lung transplant recipients remain alive and well, including 1 patient with cystic fibrosis, there have been significant problems. Twenty-five percent of the patients have died as a result of tracheal complications, and another 20% have developed delayed airway stenosis requiring special management. Thus, once again we have a clinical problem in search of

Fig 39. The common pulmonary artery of the recipient is transsected several centimeters above the pulmonic valve (left). It is not necessary to excise the distal portion of the common pulmonary artery or the right and left pulmonary artery stumps. An end-to-end anastomosis is then created between the donor and the recipient pulmonary arteries (right).



a solution, and our attention is focused on the animal laboratory and the autopsy room to develop methods of retaining or augmenting tracheal circulation for this procedure or utilizing bronchial rather than tracheal anastomoses.

Many other problems remain to be solved in the field of lung transplantation. One of the most pressing issues is the need for methods to improve lung preservation. A variety of techniques are currently utilized including simple cold immersion (which we use), flushing of the lungs with cold solutions of various composition, and cooling the entire donor with cardiopulmonary bypass before extraction of the transplantable organs. With all of these methods, the safe ischemic time is considered to be less than six hours. Extending this to 12 hours would improve the supply of organs, facilitate the logistics of transplantation, and provide the possibility of histocompatibility matching between donor and recipient.

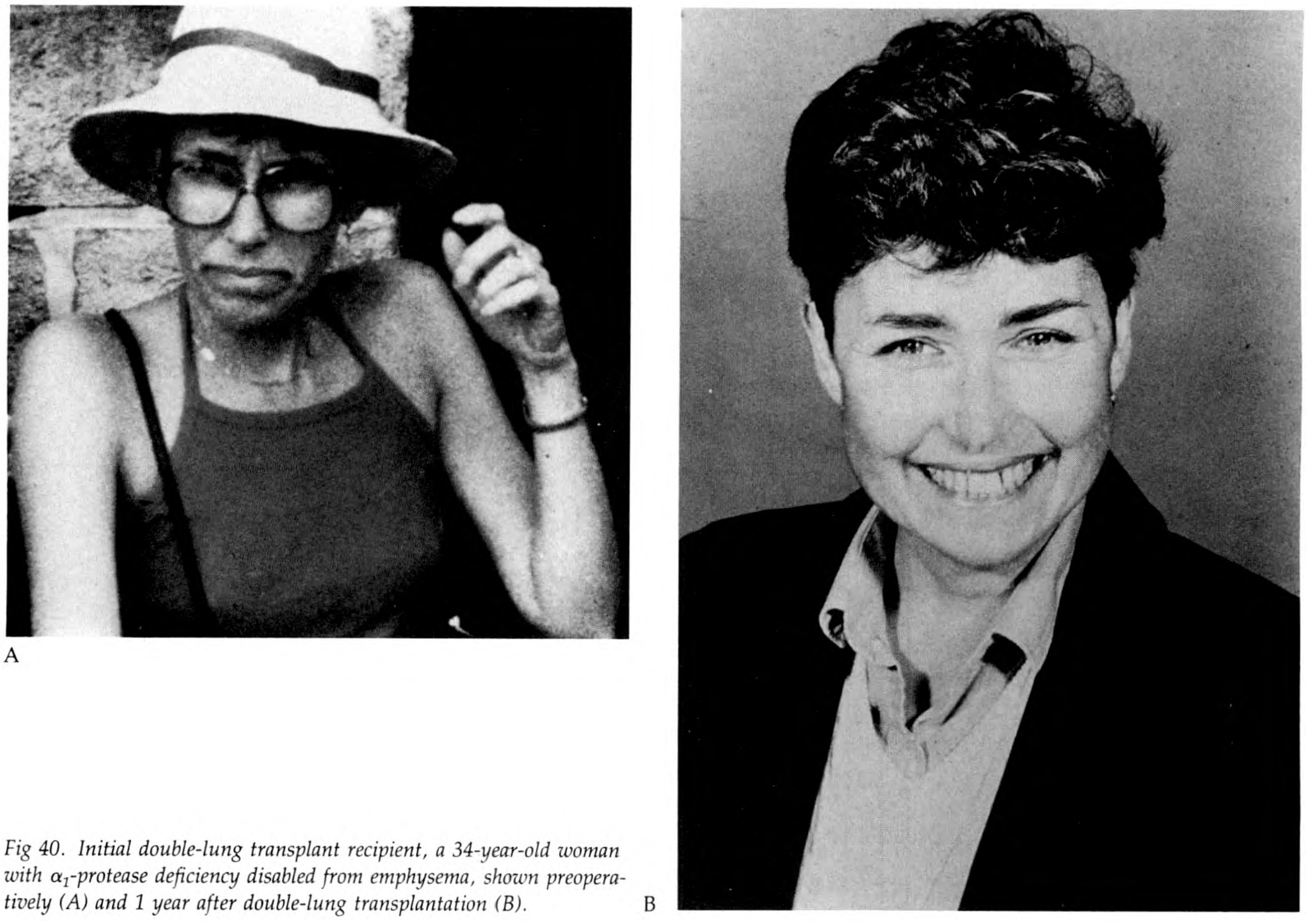

A
B

Fig 40. Initial double-lung transplant recipient, a 34-year-old woman with α_1-protease deficiency disabled from emphysema, shown preoperatively (A) and 1 year after double-lung transplantation (B).

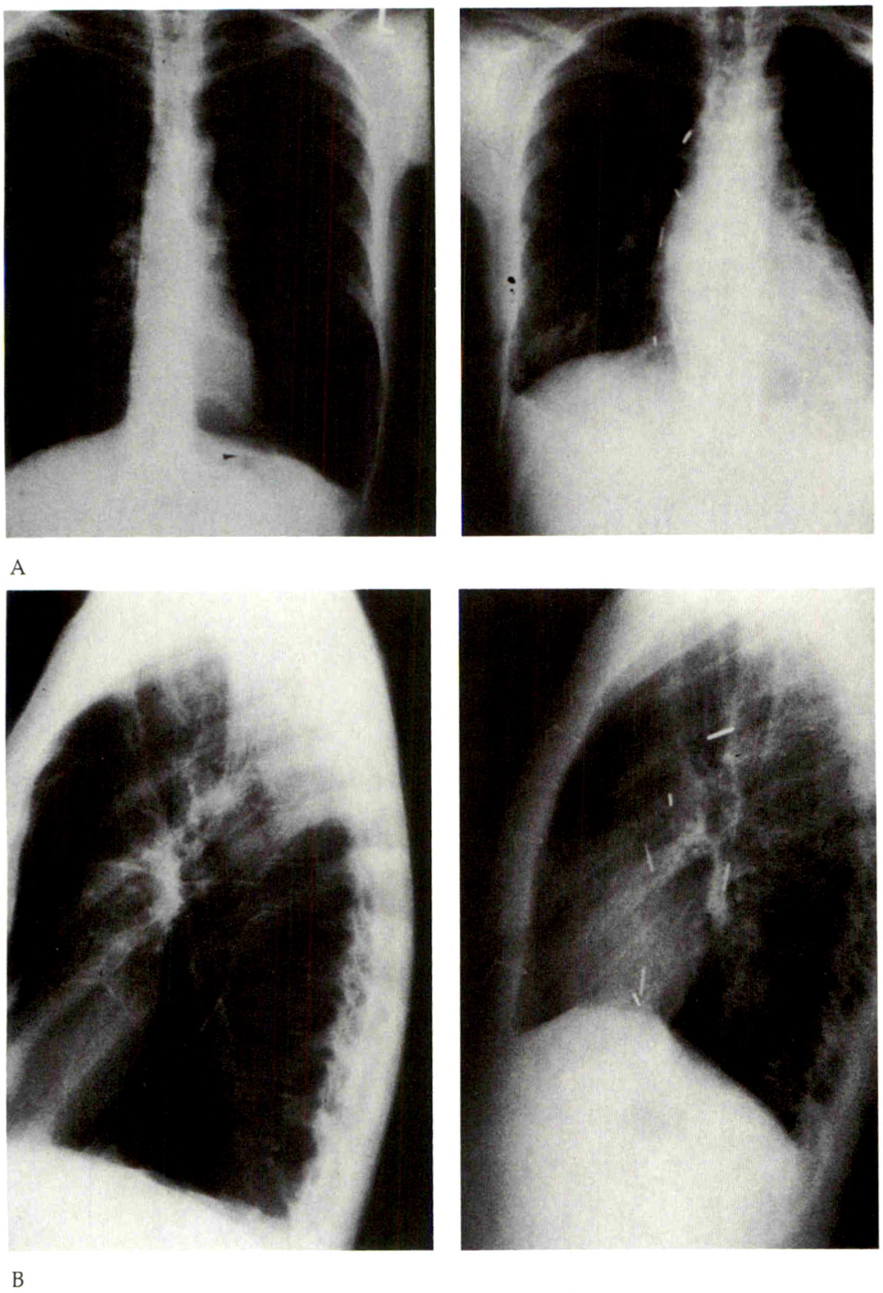


Fig 41. A. Preoperative (left) and postoperative (right) chest roentgenogram of initial double-lung recipient. The preoperative roentgenogram demonstrates the marked overexpansion of the chest wall and flattened diaphragm. The postoperative film demonstrates a normal configuration of the chest wall and diaphragm. (From [9]. Reprinted with the permission of the C.V. Mosby Company.) B. This is especially well demonstrated in the lateral view. The restoration of normal chest wall configuration occurs within weeks of transplantation.

Another unsolved problem is the diagnosis of pulmonary rejection. The diagnosis is currently made primarily on clinical grounds and on the response to a pulse dose of steroids. Transbronchial biopsy, bronchoalveolar lavage, and evaluation of peripheral blood for lymphocyte subsets are being evaluated at various centers.

There is understandable controversy as to the relative merits of the double-lung versus the heart-lung transplantation for patients with end-stage pulmonary disease. The double-lung transplantation avoids wasting a donor heart or unnecessarily removing the heart from a patient who does not need cardiac replacement. It avoids the complications due to the cardiac portion of the transplantation, and potentially permits many more transplantations to be performed for end-stage lung disease. On the other hand, the "domino" procedure has been successfully utilized. In this procedure a heart-lung block is placed into a recipient with end-stage lung disease but a good heart, and the recipient's heart is extracted and donated to another individual in need of a cardiac transplantation [11]. This procedure also avoids wasting a usable heart. The tracheal anastomosis with heart-lung transplantation has been less prone to complication than with double-lung transplantation. However, the long-term functional results after combined heart-lung transplantation have been disappointing due to the significant incidence of obliterative bronchiolitis.

It seems apparent that the era of transplantation for end-stage lung disease has arrived. The demonstration of successful transplantation has stimulated interest at many centers, and from this further progress is certain to occur. Many questions remain unanswered, many problems unsolved, providing endless opportunity for the next generation of surgical investigators.

Dr Sloan has devoted much of his career to ensure that the next generation of thoracic surgeons is well trained, well informed, and motivated to recognize, investigate, and solve many of the clinical problems that now confront us.

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The Asymptomatic Child a Long Time After the Mustard Operation for Transposition of the Great Arteries

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We studied 36 asymptomatic children 7.7 ± 2.5 years after a Mustard operation. Fifteen children had sinus rhythm on all electrocardiograms made during follow-up. Only 2 had normal 24-hour Holter recordings throughout follow-up, 6 had periods of supraventricular tachycardia, and 3 had periods of atrial flutter. The electrophysiological evaluation of sinus node function was normal in 5 of the 31 children who were studied. The behavior of the atrial myocardium was electrophysiologically abnormal in most of the children. Atrioventricular node function, on the contrary, was normal in nearly all of the children. Eleven children had normal hemodynamics. Four had severe or complete obstruction of the superior vena cava, 1 had a severe pulmonary venous obstruction, 3 had a severe left ventricular outflow tract obstruction, and 2 had a large left-to-right shunt. Only 3 children had normal hemodynamic and electrophysiological studies. We conclude that the absence of symptoms and a normal routine examination of children a long time after a Mustard operation does not exclude hemodynamic and electrophysiological abnormalities, which can sometimes be severe. In view of these disappointing results, we decided to replace the Mustard operation with the arterial switch operation in children with transposition of the great arteries.

(Ann Thorac Surg 1989;47:45–50)

Since 1964 when Mustard [1] described the venous switch operation, the life expectancy and the quality of life of many children with transposition of the great arteries have improved. The operative mortality was extremely low, and the early results were good. After long-term follow-up, however, many problems were encountered; caval obstruction, pulmonary venous obstruction, tricuspid insufficiency, and right heart failure [2–5]. A high incidence of supraventricular arrhythmias and sinus node dysfunction has been reported, as well as a high incidence of sudden death, perhaps as a result of these arrhythmias [6–8].

Between 1969 and 1984, we [9] performed the Mustard operation in our hospital in 83 children with transposition of the great arteries. There have been no operative deaths for simple transposition of the great arteries since 1977 and for complex transposition since 1980; however, late mortality has been high. Eight children died suddenly and unexpectedly. There was a strong correlation with the presence of tachyarrhythmias; 7 of these 8 children had periods of atrial flutter compared with 16% of the whole group ($p < 0.01$). Although 8 children required reoperation and 5 required implantation of a pacemaker, the remaining children have done very well.

We wanted to know more about this group of asymptomatic children. Therefore, we studied 36 of them by means of hemodynamic and electrophysiological heart catheterization. All 36 had undergone a Mustard operation more than 4 years before. The results of the study are presented here.

Material and Methods

Patients

Thirty-six asymptomatic children who had undergone a Mustard operation more than 4 years prior to the present study (mean ± SD, 7.7 ± 2.5 years) formed the study group. Based on the physical examination, 12-lead electrocardiogram (ECG), and chest roentgenogram, there was no suspicion of severe hemodynamic or electrophysiological abnormalities. Children who showed only a diminished capacity to perform competitive sports were included in the study.

Operative Technique

All the children were operated on using cardiopulmonary bypass and hypothermia. Since 1977, the superior vena cava (SVC) and inferior vena cava have been selectively cannulated and cold cardioplegia has been used. Dacron was used as the baffle material in all of the children; since 1979, the baffle has been "trouser shaped" according to the method of Quaegebeur and Brom [10]. The coronary sinus drained into the pulmonary venous atrium. The pulmonary atrium was enlarged with a pericardial patch in 10 children. Previous procedures included a Blalock–Hanlon atrial septectomy in 7 children.

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Table 1. Patient Characteristics of the Three Groups[a]

Variable	Total (n = 36)	Group 1 (n = 16)	Group 2 (n = 10)	Group 3 (n = 10)
Follow-up (yr)	4–12 (7.7)	6–12 (10)	4–9 (6.5)	4–6 (5.1)
Age at operation[b]	2 days–7.4 (1.9)	0.7–5.6 (3)	0.7–7.4 (1.6)	2 days–1.1 (0.5)
VSD				
Large	1	0	1	0
Small	9	3	4	2
LVOTO	10	4	4	2
PDB	7	2	2	3

[a] Numbers in parentheses are mean values. [b] Data are shown in years unless otherwise indicated.

LVOTO = left ventricular outflow tract obstruction; PDB = persistent ductus of Botallo; VSD = ventricular septal defect.

To judge the possible effect of surgical modifications, we divided the children into three groups based on changes in surgical policy. In group 1, the operations took place between 1969 and 1977, and were performed mainly in children older than 1 year. In group 2, the operations occurred between 1977 and 1980, and were done using cold cardioplegia and selective cannulation of the caval veins. In group 3, the operations were done between 1980 and 1984 on children younger than 1 year. The data on age, follow-up, and associated anomalies are in Table 1.

Study Protocol

All postoperative ECGs and 24-hour Holter recordings were reviewed. The ECGs were made at least once a year, and the 24-hour Holter recordings were made every 1 or 2 years. The mean number of 24-hour Holter recordings per patient was 4.7 ± 3. Seventeen children (47%) performed an exercise test with a bicycle ergometer according to the protocol described by Godfrey and colleagues [11]. A two-dimensional and Doppler echocardiogram was made on the day of catheterization.

Cardiac Catheterization

After the parents gave informed consent and after approval by the institution's committee of clinical investigation, all of the children underwent hemodynamic and electrophysiological catheterization. Most of the children were sedated with meperidine hydrochloride, 2 mg/kg of body weight, and promethazine, 1 mg/kg of body weight, administered intramuscularly. Eight children older than 12 years were sedated with diazepam given orally. The catheter was introduced percutaneously into a femoral vein and artery. In 6 patients in whom both the femoral and iliac veins were occluded, the internal jugular vein was entered percutaneously under general anesthesia.

HEMODYNAMIC STUDY. Besides the usual pressure and oxygen saturation measurements, withdrawal pressures were registered from the SVC to the inferior vena cava through the systemic venous atrium and from the main pulmonary artery to the left ventricle. The pulmonary wedge pressure was measured simultaneously with either the pressure in the pulmonary venous atrium or the right ventricular end-diastolic pressure. Cardiac index and shunt calculations were made by the dye-dilution technique. Biplane cineangiograms were made with contrast injections in the SVC and both ventricles. Volumes were calculated from the biplane angiogram utilizing Simpson's rule method [12].

ELECTROPHYSIOLOGICAL STUDY. An electrophysiological study could be performed in 31 children. A 5F quadripolar catheter was placed at the junction between the SVC and the systemic venous atrium. Four surface ECGs (I, II, aVF, and V_1) and the femoral arterial pressure were recorded throughout the study. Recordings were performed with a Siemens-Elema Mingograph with a paper speed of 100 or 250 mm/s. A Medtronic 5325 stimulator was used for pacing. The amplitude of the stimuli delivered was twice the threshold with a pulse width of 1.8 ms. Electrophysiological measurements included the following: corrected sinus node recovery time [13], sinoatrial conduction time [13], AV node Wenckebach response to atrial pacing, and effective refractory periods of the atrium and AV node. Values more than two standard deviations above the mean value for children with normal hearts were considered abnormal [14, 15].

Statistical Analysis

Statistical analysis was performed with the χ^2 test. A p value of less than 0.05 was considered significant. Results were expressed as the mean ± one standard deviation.

Results

Electrocardiogram

Fifteen children (42%) were in sinus rhythm during the entire follow-up period (Table 2). Although the incidence of sinus rhythm was the highest in group 3 (60%), the differences between the three groups were not significant. Eighteen children had at least one period of AV junctional rhythm on their ECG, alternating with atrial rhythm or atrial flutter in 6 children.

24-Hour Holter Recording

Only 2 (6%) children had no abnormalities on all of their 24-hour Holter recordings (see Table 2). The periods of

Table 2. Children With Specific Rhythm or Arrhythmia on Electrocardiograms and 24-hour Holter Recordings Made During Follow-up (n = 36)

Variable	ECG	Holter
Sinus rhythm	15 (42%)	2 (6%)
AV junctional rhythm	18	21
Atrial rhythm	6	6
Sinus arrest	3	12
SVT	0	6
Atrial flutter	3	3
PAC	3	13[a]
PVC	0	3[a]

[a] These patients had more than ten contractions per hour.

AV = atrioventricular; ECG = electrocardiogram; PAC = premature atrial contraction; PVC = premature ventricular contraction; SVT = supraventricular tachycardia.

sinus arrest were longer than 1.8 s in 6 children. (Sinus arrest up to 1.8 s is also seen in healthy children [16].) Most children had more than one type of arrhythmia during follow-up. The incidence and type of arrhythmias did not differ significantly between the three groups. However, atrial flutter was present only in group 1.

Exercise Test

The exercise capacity ranged from 59% to 100% (mean capacity, 75%) of normal for length and sex. Premature atrial contractions developed in 3 children during exercise; 2 remained in AV junctional rhythm throughout the exercise test.

Echocardiogram

A complete two-dimensional and Doppler echocardiogram was obtained in 26 of the 36 children. An obstruction of the systemic venous return was suspected by pulsed Doppler echocardiography because of nonphasic disturbed blood flow during diastole in 6 of the 9 patients with substantial pressure gradients at cardiac catheterization. A complete echocardiogram was available for 4 patients with pulmonary venous channel stenosis, all demonstrating a narrowed channel (less than 11 mm), with flow disturbance in the inflow of the atrium. A major left ventricular outflow tract obstruction was detected by echocardiography in all 7 patients with pressure gradients higher than 25 mm Hg at cardiac catheterization. Baffle leak flow was demonstrated in 4 patients and was missed in 4, in whom the shunt was less than 25% of the pulmonary circulation.

Hemodynamic Study

No hemodynamic abnormalities were found in 11 children (31%) (Table 3). The rest often had more than one abnormality. We found no significant differences between the three groups in the incidence of hemodynamic abnormalities separately or combined. In group 3, however, no severe baffle obstructions were found.

CAVAL OBSTRUCTIONS. In 4 children, the obstruction was severe (greater than 10 mm Hg) or complete. All of the children had good runoff through the azygos vein to the inferior vena cava. None of the children with an SVC obstruction had a protein-losing enteropathy.

PULMONARY VENOUS OBSTRUCTION. A pressure difference of more than 10 mm Hg between the pulmonary artery wedge pressure and either the right ventricular end-diastolic pressure or the pulmonary venous atrial pressure was found in 1 child. Of the 10 children in whom the pulmonary venous atrium was enlarged, 1 had a moderate pulmonary venous obstruction.

LEFT VENTRICULAR OUTFLOW TRACT OBSTRUCTION. Of the 7 children with left ventricular outflow tract obstruction, 6 had pressure differences over the left ventricular outflow before operation. The stenosis remained the same in 4 and increased in 2. In 4 children with a preoperative obstruction, the pressure difference disappeared after the Mustard operation.

BAFFLE LEAKAGE. The leakage was located mostly in the vicinity of the SVC or inferior vena cava. The left-to-right shunt constituted more than 25% of the pulmonary flow in 2 children.

TRICUSPID INSUFFICIENCY. Two children showed moderate tricuspid insufficiency on the right ventricular cineangiogram.

Table 3. Results of Hemodynamic Studies in the Three Groups

Variable	Total (n = 36)	Group 1 (n = 16)	Group 2 (n = 10)	Group 3 (n = 10)
Normal	11 (31%)	6	1	4
SVC obstruction				
5–10 mm Hg	4	1	2	1
>10 mm Hg	4	3	1	0
IVC obstruction				
5–10 mm Hg	2	1	0	1
>10 mm Hg	0	0	0	0
PV obstruction				
5–10 mm Hg	5	2	1	2
>10 mm Hg	1	0	1	0
LVOTO				
25–50 mm Hg	4	2	1	1
>50 mm Hg	3	1	1	1
Baffle leakage				
<25%	8	2	4	2
>25%	2	0	2	0
Tricuspid insufficiency	2	0	1	1
Cardiac index (L/min/m^2)	3.3 ± 0.7	3.5 ± 0.8	3.1 ± 0.4	3.2 ± 0.7

IVC = inferior vena cava; LVOTO = left ventricular outflow tract obstruction; PV = pulmonary venous; SVC = superior vena cava.

Table 4. Electrophysiological Results in the Three Groups

Variable	Total	Group 1	Group 2	Group 3
CSNRT (n = 31)				
<275 ms	5 (16%)	1	2	2
275–550 ms[a]	15	9	2	4
>550 ms[a]	11	4	4	3
Secondary pauses[a]	8	5	1	2
Abnormal escape[a]	16	10	3	3
Entrance block[a]	8	3	2	3
Atrial standstill	1	1	0	0
SACT (n = 24)				
<200 ms	6	2	3	1
>200 ms[a]	4	1	1	2
Not determinable	14	7	1	6
Wenckebach (n = 31)				
<350 ms	27 (87%)	13	6	8
>350 ms[a]	4	1	2	1
AVERP (n = 27)				
Normal[b]	26 (96%)	11	6	9
Prolonged[a]	1	0	1	0
AERP (n = 27)				
Normal[b]	10 (37%)	5	2	3
Prolonged[a]	17	6	5	6

[a] A statistical analysis was done, and there was no significant difference between groups. [b] Normal values are dependent on cycle length.

AERP = atrial effective refractory period; AVERP = atrioventricular node effective refractory period; CSNRT = corrected sinus node recovery time; SACT = sinoatrial conduction time.

CARDIAC FUNCTION. One child had a cardiac index lower than 2.5 L/min/m^2. Right ventricular ejection fraction could be measured in 13 children. The mean ejection fraction was 57% ± 12%. Three children had an ejection fraction lower than 45%.

Electrophysiological Study

An electrophysiological study could be performed in 31 children (Table 4). Nonsustained tachycardia from atrial pacing or from atrial extrastimuli given during sinus rhythm developed in 10 children (32%): supraventricular tachycardia in 6; atrial flutter in 3; and a wide QRS tachycardia, possibly of ventricular origin, in 1. The correct electrophysiological mechanism could not be analyzed because only one electrode catheter was used.

The number and the severity of the electrophysiological abnormalities did not differ significantly between the three groups (see Table 4). Of the 11 children in whom no hemodynamic abnormalities were found, 4 had severe abnormalities of the sinus node. These abnormalities were detected during the electrophysiological study as well as in the 24-hour Holter recordings. Four others had moderately abnormal electrophysiological studies and arrhythmias. Only 3 children had both normal hemodynamic and electrophysiological studies.

SINUS NODE. The response of the sinus node to atrial pacing was very abnormal in most of the children. The corrected sinus node recovery time was within the normal range in only 5 children (16%). In 2 of these children, this could have been due to an entrance block of the sinus node. The corrected sinus node recovery time was moderately abnormal in 15 and severely abnormal in 11 with a maximum time of 2,690 ms. More striking was the abnormal behavior of the sinus node. Secondary pauses were seen in 8 children, abnormal escape rhythm in 16, and entrance block in 8. In 1 child with AV junctional escape, an atrial standstill of 28 s was found. In 14 children, the sinoatrial conduction time could not be calculated either because of non-reset of the sinus node or the presence of pronounced sinus arrhythmia.

ATRIOVENTRICULAR NODE. Atrioventricular node function was normal in most of the children.

ATRIUM. The atrium reached refractoriness before the AV node in 72% of the children. Only 20% of normal children show this phenomenon [14].

Late Deaths

Three children died suddenly during follow-up after cardiac catheterization. One child had normal hemodynamics but severe abnormalities of the sinus node with periods of atrial flutter on the 24-hour Holter recordings. She died during exercise, despite having an AAI pacemaker and receiving antiarrhythmic drug treatment. The other 2 children had a pulmonary venous obstruction with a pressure difference of 5 to 10 mm Hg. One of them also had periods of atrial flutter.

Comment

The results of this study show that most children who have undergone a Mustard operation, even if they are asymptomatic and seem to be doing well, have major hemodynamic and electrophysiological abnormalities. We cannot predict what the consequences of these findings will be for the children we studied, who are asymptomatic at present. Obstruction of the SVC is well tolerated if there is good collateral venous drainage; however, problems (due to intestinal lymph congestion, for example) can be expected. If moderate pulmonary venous obstruction is present in childhood, progressive narrowing with growth seems probable. A residual left-to-right shunt will possibly, by its volume load, increase the chance of arrhythmias developing in the already compromised atrium. We, therefore, believe that hemodynamic problems can be expected in these asymptomatic children in the future.

Hayes and Gersony [17] and Duster and associates [18] reported that the incidence of arrhythmias increased with longer follow-up. Therefore, it can be anticipated that the arrhythmias and the electrophysiological abnormalities in our patients will worsen and probably will become symptomatic with a much longer follow-up. Southall and co-workers [19] cautioned that the incidence of arrhythmias created by operative intervention should not be overestimated, because children with normal hearts also show arrhythmias on 24-hour Holter recordings and because arrhythmias are already present preoperatively in some children with congenital heart disease. We did not perform 24-hour Holter recordings preoperatively, but all the children had sinus rhythm preoperatively on the surface ECG compared with 42% postoperatively. The arrhythmias detected on the 24-hour Holter recordings were more severe than those described by Southall and colleagues [16] in normal children. Atrioventricular junctional rhythm was seen for several hours, and occasionally throughout most of the 24 hours. Only more than ten premature beats per hour was considered abnormal. Supraventricular tachycardia and atrial flutter, as found in our patients, are not seen in healthy children. Therefore, we believe we do not overestimate the incidence of arrhythmias after the Mustard operation.

Many surgical modifications have been described to reduce the incidence of hemodynamic and electrophysiological problems after the Mustard operation [20–22]. Many of these modifications, eg, selective SVC cannulation, the trouser-shaped patch, and superficial stitching around the sinus node area, have been applied in our hospital. Despite this, the hemodynamic and electrophysiological results did not improve significantly, as shown by comparison of the three surgical groups. Atrial flutter was seen only in group 1, but this is as likely to be the result of the longer postoperative period [17, 18] as the result of the changes in surgical technique. The absence of severe baffle obstructions in group 3 can likewise be explained by the shorter postoperative period.

The incidence of sudden death was very high in our patients compared with the incidence of sudden death reported in the literature [6]. Deanfield and associates [23] found no correlation between the presence of arrhythmias and sudden death in their prospective study. Three of our children died during follow-up after catheterization. Two of them had periods of atrial flutter, as did 7 of 8 children who died suddenly before the study was started. Unlike Deanfield and colleagues [23], we found that atrial flutter seemed to increase significantly the risk of sudden death in our patients. Of the 3 children who died in our series, 1 was not known to have atrial flutter. The other 2 died during exercise or during proven tachycardia. Ventricular fibrillation as a result of 1:1 conduction of atrial flutter could well have been the cause of sudden death in these children.

The arterial switch operation, presented in 1975 by Jatene and co-workers [24] as an anatomical correction for transposition of the great arteries, had such a high operative mortality at first that it was not then an alternative for the Mustard operation. However, the operative mortality of the arterial switch operation has decreased considerably during recent years. Quaegebeur and colleagues [25] and Radley-Smith and Yacoub [26] reported a 12% and 9% operative mortality, respectively. Late mortality was 5% and 0%, respectively. Although much fewer data are available on the long-term follow-up of the arterial switch operation than on the Mustard operation, it seems that arrhythmias are rare and hemodynamic problems are less frequent than after Mustard's operation [25–28].

We conclude that even children who seem to be doing well a long time after a Mustard operation have unexpected hemodynamic and electrophysiological abnormalities that could well deteriorate during further follow-up. Moreover, the results point out that the absence of symptoms combined with no or minor abnormalities at the physical examination and on the ECG and chest roentgenogram do not mean that the child is really well. Only cardiac catheterization and repeated 24-hour Holter recordings together with two-dimensional and Doppler echocardiography can exclude abnormalities. Considering the disappointing results of the Mustard operation as shown in this study, and in view of the recent encouraging results of the arterial switch operation, we considered it justified at our institution to replace the Mustard operation with the arterial switch operation for children with simple and complex transposition of the great arteries.

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REVIEW OF RECENT BOOKS

Clinical Cancer Monographs, Vol 1. Cancer of the Oesophagus

Edited by Hugoe R. Matthews, John A. H. Waterhouse, Jean Powell, Christopher C. McConkey, and Janet E. Robertson
New York, Stockton Press, 1987
184 pp, illustrated, $80.00

Reviewed by Richard M. Peters, MD

This is a report of incidence and survival of carcinoma of the esophagus over a 25-year period (1957 to 1981) in the Midlands region of Great Britain. The report is a compilation of statistics on 4,680 patients with carcinoma confined to the esophagus (hypopharynx and cardia carcinomas are excluded). The data were collected by trained nurse reviewers and a number of validation procedures were used. Only 0.13% of patients were lost to follow-up.

The book is mostly tables and graphics with brief interpretations of findings. A number of interesting facts come out of the analyses. The risk of cancer of the esophagus has increased in each of the younger age groups as compared with elders. This increase is in cancer of the middle and lower thirds of the esophagus. The male-female ratio is equal for age groups up to 50 years, when incidence in men starts to exceed that in women. The relative incidence of adenocarcinoma has increased, and is now 11.9%.

The results of therapy are discouraging. There is only a 3% 5-year survival, which has not changed over the 25 years of the data collection. Fewer than 15% of patients are alive at 1 year, and half of these die in the second year. Squamous is the most favorable histological type of carcinoma.

Among all patients, 48.8% had treatment designed to decrease the amount of tumor; 24.4% underwent operation (21.5% of males, 28.1% of females). In these groups the 1-month mortality was 10%.

This book reinforces the terrible outcome of this disease, and the fact that it is not disappearing but rather increasing in the Midlands area of England. All forms of therapy have overall poor outcome. The data do not show greater success for operation than for radiation therapy. The combination of operation and irradiation may be best.

This book will serve as a reference for evaluating population demographics, the incidence of cancer of the esophagus, and the effects of treatment. It is a library reference more than a book for an individual's library.

San Diego, California

Improved Early Results After Aortic Valve Replacement: Analysis by Surgical Time Frame

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Primary aortic valve replacement was performed in 430 patients. It was an isolated procedure in 339 and was combined with coronary artery bypass grafting in 91. Of these patients, 282 underwent operation from 1970 through 1976 (time frame 1) and 148 from 1980 through 1985 (time frame 2). They were divided into subgroups by age, New York Heart Association functional class, combined coronary artery bypass graft, and valvular lesion. Overall hospital mortality was 7.7% (time frame 1 = 10.6% versus time frame 2 = 2.0%; $p < 0.01$). Overall, functional class III or IV was the strongest predictor of hospital mortality ($p < 0.001$). Association of coronary artery bypass graft was the next strongest predictor of hospital mortality ($p < 0.01$), and it retained its predictive value in time frame 2. Overall, hospital mortality was higher in patients older than 55 years (10.5% versus 3.5%; $p < 0.05$). There were no hospital deaths in patients younger than 55 years in time frame 2. Type of valvular lesion was not a predictor of hospital mortality. Hospital mortality in patients receiving cardioplegia was 2%. Cardioplegia use has lessened the effect of age and functional class as predictors of hospital mortality after primary aortic valve replacement. Earlier operation in time frame 2 played a substantial role in the overall improvement of early results.

(Ann Thorac Surg 1989;47:51–6)

Contemporary aortic valve replacement can be performed with a very low surgical risk. The impressive decline in operative mortality over the years has been ascribed mainly to changes in myocardial protection techniques [1, 2]. Various reports have analyzed, sometimes extensively, the effect of multiple preoperative and intraoperative variables on hospital mortality. Age [2], associated coronary artery bypass grafting (CABG) [3], valvular lesion [4], and preoperative New York Heart Association functional class [4] are among those reported as being predictive of premature hospital death after aortic valve replacement. When large series extending over a long time span are reviewed, the year of operation is an important predictor of hospital mortality [3]. In this report, we analyze the effects of age, valvular lesion, preoperative functional class, and combined CABG on hospital mortality after primary aortic valve replacement, and compare them in two widely separated time frames with the purpose of identifying changes in their predictive value over the years.

Material and Methods

The medical records of patients receiving primary aortic valve replacement in two different time frames of our practice were reviewed: aortic valve replacement was performed between 1970 and 1976 (time frame 1) in 282 patients and between 1980 and 1985 (time frame 2) in 148 patients. The operations performed between 1977 and 1979 were excluded to amplify differences between the results in the two groups of patients. Only patients in whom a Björk–Shiley spherical-disc valve was used were included in the study. Ninety-one of the 430 patients had CABG combined with aortic valve replacement. The age of the patients ranged from 20 to 80 years (mean age, 55 ± 14 years). Pure aortic stenosis was present in 121 patients, pure aortic insufficiency in 112, and mixed lesions in 197.

The patients were divided into subgroups by age (20 through 54 years, 55 through 64 years, 65 to 80 years), by preoperative New York Heart Association functional class (I and II, III and IV), by associated CABG (yes, no), by type of valvular lesion (stenosis, insufficiency, mixed), and by time frame (time frame 1, time frame 2). The separation of patients by time frame allowed us also to identify differences in the relative prevalence of the clinical characteristics under examination.

Hospital mortality was defined as death occurring during the hospital stay or within 30 days of the operation. All patients older than 40 years of age underwent preoperative coronary arteriography regardless of the presence of angina, and all stenoses greater than 50% of major coronary branches were bypassed. Hospital mortality for each subgroup was calculated in the overall population as well as in the two different time frames.

Perfusion times, cross-clamp times, and methods of myocardial protection used in the two time frames were identified, and hospital mortality was calculated according to them. When multidose cardioplegia was used, a nonoxygenated crystalloid solution was employed and was always associated with epicardial cooling with saline slush. When regional hypothermia alone was used, the pericardial cavity and the left ventricular cavity were cooled with a 4°C electrolyte solution.

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Table 1. Distribution of Patients by Time Frame in Each Subgroup

	Time Frame 1 (n = 282)			Time Frame 2 (n = 148)	
Variable	No.	%	p Value[a]	No.	%
Age (yr)					
20–54	112	40	<0.05	61	41
55–64	109	39		40	27
65–80	61	22		47	32
Functional class					
I, II	87	31	<0.001	109	74
III, IV	195	69		39	26
Coronary bypass					
No	214	76	<0.05	125	84
Yes	68	24		23	16
Valvular lesion					
AS	81	29	NS	40	27
AI	71	25		41	28
AS + AI	130	46		67	45

[a] This value represents significance between the two time frames.

AI = aortic insufficiency; AS = aortic stenosis; NS = not significant.

Continuous variables were expressed as the mean ± standard deviation of the mean. Comparison between discrete variables was performed univariately by the χ^2 or Fisher exact test, as appropriate. Stepwise logistic regression analysis was used to assess the independent predictive value of hospital death for all variables under study.

Results

Patient characteristics were compared between the two time frames. The types of valvular lesions did not differ, but age, functional class, and incidence of associated CABG showed a significant difference in their relative prevalence (Table 1). Patients in time frame 2 were slightly older, but a higher proportion of patients in time frame 1 had advanced cardiac disability. The number of patients needing associated CABG decreased in time frame 2.

Hospital mortality was 7.7% (33 patients) in the whole population and was lower in time frame 2 (3/148 [2.0%] versus 30/282 [10.6%]; $p < 0.01$). Statistical analysis identified time frame as an independent predictor of hospital mortality ($p < 0.05$). The other independent predictors of hospital mortality were functional class III or IV ($p < 0.05$), associated CABG ($p < 0.05$), and age ($p < 0.05$). The type of valvular lesion did not influence hospital mortality.

In Table 2, the difference in hospital mortality between subgroups is analyzed univariately for each variable, both on the whole population and after subdivision into time frames. A dramatic decrease in hospital mortality for each age subgroup was observed in time frame 2, with no deaths in patients less than 55 years old. In either time frame, the increase in hospital mortality was at age 55 years, with little change thereafter.

Hospital mortality was higher for patients in functional class III or IV than for patients in functional class I or II (12.0% versus 2.6%; $p < 0.001$), the difference being mainly due to time frame 1. Hospital mortality in time frame 2 was similar for patients in the low as well as the advanced functional classes.

The strong effect of associated CABG on hospital mortality (15.4% versus 5.6%; $p < 0.01$) was evident in both time frames, although it was statistically significant only in time frame 1. In time frame 2, CABG was associated with an almost threefold mortality, but statistical significance was not achieved because of the small numbers.

Table 3 shows that in patients in the low functional classes, hospital mortality increased with age but behaved differently according to the presence of combined CABG. In isolated aortic valve replacement, hospital mortality remained low up to age 65 years (1.2% to 2.3%) and then more than doubled (5.7%). With associated CABG, hospital mortality was high only in the youngest subgroup, with a relative risk of almost seven times, but this difference was not statistically significant because of the small number of patients ($p = 0.2$).

In the advanced functional classes, hospital mortality was higher, as expected. In isolated aortic valve replacement, the increase in hospital mortality was at age 55 years (2.9% to 11.8% to 12.2%). In the advanced functional class subgroup, the impact of associated CABG was more evident: the relative risk for age groups 20 through 54 years and 55 through 64 years was higher than in the low functional class subgroup, and the difference in mortality was significant between ages 20 and 64 years ($p < 0.05$).

When the same data from Table 3 were arranged by time frame (Table 4), it was evident that the significant increase in hospital mortality caused by associated CABG

Table 2. Hospital Mortality in Each Subgroup for Total Population and for Each Time Frame

	Time Frame 1			Time Frame 2			Total		
Variable	No.	%	*p* Value	No.	%	*p* Value	No.	%	*p* Value
Age (yr)									
20–54	6/112	5.4	0.05	0/61	0	NS	6/173	3.5	0.05
55–64	16/109	14.7		1/40	2.5		17/149	11.4	
65–80	8/61	13.1		2/47	4.3		10/108	9.3	
Functional class									
I, II	3/87	3.4	0.01	2/109	1.8	NS	5/196	2.6	<0.001
III, IV	27/195	13.8		1/39	2.6		28/234	12.0	
Coronary bypass									
Yes	13/68	19.1	0.02	1/23	4.3	NS	14/91	15.4	<0.01
No	17/214	7.9		2/125	1.6		19/339	5.6	
Valvular lesion									
AS	11/81	13.6	0.25	2/40	5.0	0.21	13/121	10.7	0.20
AI	4/71	5.6		1/41	2.4		5/112	4.5	
AS + AI	15/130	11.5		0/67	0		15/197	7.6	

AI = aortic insufficiency; AS = aortic stenosis; NS = not significant.

in patients with advanced cardiac disability could be ascribed totally to deaths occurring in time frame 1.

Changes in the intraoperative variables under examination are illustrated in Table 5. Myocardial protection in time frame 1 included continuous coronary perfusion in 52% of the patients (146/282), regional hypothermia in 34% (96/282), and simple hypothermic arrest in 14% (40/282). Over the years there has been a transition from one technique to another, the latest being regional hypothermia. In time frame 2, cardioplegia was used in 69% of the patients (102/148) and regional hypothermia, in 46 (31%). This reflects the personal preference of one surgeon in the group, who preferred regional hypothermia over cardioplegia. Hospital mortality was 2% (2/102) with the use of cardioplegia (time frame 2 only) and 13% (19/146) and 10% (4/40) for coronary perfusion and simple hypothermic arrest, respectively (time frame 1 only). Overall mortality when regional hypothermia was used was 5.6% (8/142).

The difference between the four mortality rates was significant ($p < 0.01$). Regional hypothermia is the only method used in both time frames; hospital mortality was 7.3% (7/96) in time frame 1 and 2.2% (1/46) in time frame 2. The difference was not significant ($p < 0.2$). Mean perfusion times and cross-clamp times were longer in time frame 2, but only cross-clamp times were significantly different ($p = 0.02$).

Comment

In the last decade, aortic valve replacement has been increasingly performed in elderly patients, with some reports documenting optimal results in patients aged 70 years or more [5, 6]. This trend is evident in our series as well, with a significant increase in the number of patients older than 65 years in recent years at the expense of middle-aged patients.

The other significant trend we identified was a very substantial decrease in the number of patients in the

Table 3. Hospital Mortality in the Overall Population With Age, Functional Class, and Associated Coronary Artery Bypass Subgroups Combined

		Functional Class I, II			Function Class III, IV		
Age (yr)	Bypass	Deaths (%)	*p* Value	Relative Risk[a]	Deaths (%)	*p* Value	Relative Risk[a]
20–54	No	1/82 (1.2)	0.2	6.7	2/70 (2.9)	0.02	7.6
	Yes	1/12 (8.3)			2/9 (22.2)		
55–64	No	1/43 (2.3)	0.5	0	8/68 (11.8)	0.02	3.0
	Yes	0/15 (0)			8/23 (34.8)		
65–80	No	2/35 (5.7)	0.6	0	5/41 (12.2)	0.9	1.1
	Yes	0/9 (0)			3/23 (13.0)		

[a] This is the relative risk of death for aortic valve replacement alone versus aortic valve replacement plus coronary artery bypass grafting.

Table 4. Hospital Mortality in Two Time Frames With Age, Functional Class, and Associated Coronary Artery Bypass Subgroups Combined

		Functional Class I, II				Functional Class III, IV			
		Deaths in Time Frame 1		Deaths in Time Frame 2		Deaths in Time Frame 1		Deaths in Time Frame 2	
Age (yr)	Bypass	No.	%	No.	%	No.	%	No.	%
20–54	No	1/32	3.1	0/50	0	2/61	3.3	0/9	0
	Yes	1/10	10.0	0/2	0	2/9	22.2	0/0	0
55–64	No	0/17	0	1/26	3.8	8/61	13.3	0/7	0
	Yes	0/9	0	0/6	0	8/22	36.4	0/1	0
65–80	No	1/16	6.3	1/19	5.3	5/27	18.5	0/14	0
	Yes	0/3	0	0/6	0	2/15	13.3	1/8	12.5

advanced functional classes. This is in accordance with other reports [4] and reflects the changing timing of surgical referral, partly a result of the improved noninvasive assessment of ventricular function; currently operation is indicated by demonstration of deranged physiology and deteriorating ventricular function rather than worsening symptomatic status [2].

The number of associated CABG procedures has also significantly decreased in recent years, probably because of the availability of percutaneous transluminal coronary angioplasty. It is conceivable that a certain number of patients may have undergone percutaneous transluminal coronary angioplasty at a time when aortic valve disease was not clinically evident or was hemodynamically insignificant and, therefore, they would not have become candidates for a CABG procedure at the time of aortic valve operation. Precise data are not available to substantiate this hypothesis.

In our series, the surgical population has not changed significantly in terms of type of valvular lesion.

The effect of age on hospital mortality is variable in different reports. Scott and colleagues [4] found age to be an independent predictor of hospital mortality after aortic valve replacement, although it was weaker than advanced functional class. In the Veterans Administration Valve Study [7], however, age was not a predictor of hospital mortality after aortic valve replacement, possibly because other variables correlated with age, such as three-vessel coronary artery disease, carried in their analysis the same prognostic information. In a prospective study of patients operated on between 1982 and 1984, on the other hand, Christakis and co-workers [2] found age to be the only independent predictor of hospital mortality after aortic valve replacement.

In our experience, hospital mortality increased with age, and statistical analysis identified age as an independent predictor of hospital mortality. We observed a striking decrease in hospital mortality in the current time frame, in which no patient younger than 55 years died as a result of the operation. In both time frames, the significant increase in hospital mortality was at age 55 years, a finding suggesting that the relationship between hospital mortality and age is not linear.

Advanced functional class was a strong predictor of hospital mortality in our patients; in the whole population, hospital mortality in patients in functional class III or IV was more than quadruple that in patients in functional class I or II. This strong effect is evident only in the early time frame; in recent years, mortality was very similar in patients with and without advanced cardiac disability. The evidence that advanced preoperative functional class influences early results after aortic valve replacement has been reported by others [4] and has been known for several years, which contributes to the general attitude toward operating earlier. In the current time frame, 74% of our patients were in the low functional classes, one factor that certainly contributed to the improved results.

Association of CABG carried an increased risk of hospital mortality in our patients. This was evident in both

Table 5. Hospital Mortality by Time Frame According to Cardiopulmonary Bypass Times and Methods of Myocardial Protection

	Time Frame 1[a]		Time Frame 2[b]	
Method	No.	%	No.	%
Coronary perfusion	19/146	13	...	...
Hypothermic arrest	4/40	10	...	...
Regional hypothermia	7/96	7.3	1/46	2.2
Cardioplegia	...	...	2/102	2.0

[a] Perfusion time, 107.8 ± 45.7 min; cross-clamping time, 72.5 ± 22.7 min.

[b] Perfusion time, 113.5 ± 39.5 min; cross-clamping time, 78.8 ± 24.6 min.

time frames. The Veterans Administration Valve Study [7] identified the presence of three-vessel coronary artery disease as the most powerful independent predictor of hospital mortality after aortic valve replacement, whereas patients with single-vessel and double-vessel disease experienced a mortality not significantly higher than those with no coronary disease at all. Cohn and associates [3] found that patients with combined aortic and coronary disease have an increased operative risk after aortic valve replacement. Even though improving results of aortic valve replacement in the current time frame were particularly evident in this subset, a significant difference in hospital mortality existed between patients undergoing isolated aortic valve replacement and aortic valve replacement with combined CABG. Similar observations are suggested by results at the Cleveland Clinic; in that experience [8], hospital mortality after aortic valve replacement in the current period doubled when CABG was associated.

Our results are in accordance with these observations. In the current time frame, hospital mortality is still about two and a half times higher when CABG is associated. In addition, we found that CABG represented a risk factor particularly in the younger age groups, especially those patients in the advanced functional classes. A similar trend emerges in the data of Craver and colleagues [5]. In their series, patients younger than 70 years old with associated CABG experienced the same hospital mortality as elderly patients with or without associated CABG. The difference observed did not attain statistical significance, however, and only indicated a trend.

A dramatic decrease in hospital mortality has been reported by virtually all other reports analyzing changing results of aortic valve replacement [3–5]. In the experience of Cohn and co-workers [3], the decrease was more impressive for patients with associated CABG, and the change was attributed to the use of cardioplegia. A similar deduction was made by Czer and associates [9] in a recent report, in which they suggested that the use of cardioplegia reduces hospital mortality exclusively in patients with bypassed or unbypassed coronary disease. On the other hand, Scott and colleagues [4] reported decreased hospital mortality in their more recent surgical period only in patients with aortic insufficiency. In that series, monodose cardioplegia only was used in 26% of the patients, and a possible salutary effect of this method of myocardial protection was suggested by their data only in patients with aortic insufficiency. The similar effect of recent surgical time frame and use of cardioplegia on the same subset of patients may indicate a link between the two variables.

In our series, the effect of advanced functional class and age on hospital mortality has decreased considerably in the current time frame together with the remarkable decrease in the overall surgical risk. Use of multidose cardioplegia associated with epicardial cooling is the major change in technique that our group has adopted since 1980. In a previous report analyzing results of aortic valve replacement performed between 1970 and 1979 [10], we found the overall hospital mortality for a population of patients similar to the present one to be 8.6%. In that series cardioplegia was not used, and a question was raised whether the results might have been better with cardioplegia as opposed to the epicardial and intracavitary left ventricular cold irrigation used in the most recent years of that series after abandonment of continuous coronary perfusion.

From 1980 on, cardioplegia was used in 69% of the patients in the present series and was associated with a hospital mortality of only 2%. However, when regional hypothermia was used alone in time frame 2, it was associated with a low hospital mortality also (2.2%). These data may suggest that other factors besides cardioplegia play a role in the achievement of better results. Perfusion times and cross-clamp times have increased in recent years, perhaps because of a trend toward more extensive revascularization, and cannot explain the improving results. Earlier operation, observed in the current time frame, is of considerable importance because preoperative functional class is related to the tolerance of the myocardium to the ischemic insult [11].

Many other variables may have influenced the better results, such as the general improvement in medical care, especially in the early postoperative period, and better anesthesia techniques.

In conclusion, the association between recent time frame and use of cardioplegia seems to suggest a primary role for this technique of myocardial protection in the dramatic changes in early results observed in recent years, especially in older patients and patients with advanced cardiac disability. Earlier operation also plays a substantial role in the observed overall improvement. Even if less than before, the effect of bypassed or unbypassed coronary disease on hospital mortality is still disturbing. As pointed out by Czer and associates [9], coronary disease may amplify the supply–demand imbalance of patients with aortic valve disease, thereby making the left ventricle extremely susceptible to even minor breaks in myocardial protection technique or to the effect of incomplete revascularization.

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REVIEW OF RECENT BOOKS

Therapy of Lung Metastases. Proceedings of the Symposium "Die Therapie von Lungen-metastasen im interdisziplinaren Konzept," Heidelberg, June 1986
Edited by P. Drings and I. Vogt-Moykopf
Basel, Switzerland, Karger, 1988
221 pp, illustrated, $44.75

Reviewed by Alex G. Little, MD

This book contains the proceedings of a symposium on the therapy of lung metastases held in Germany in 1986 and is organized into three sections. The first section deals with basic considerations such as biology and pathology, the second section presents an overview on the surgical, medical, and radiation therapy treatments of lung metastases, and the final section deals with treatment of pulmonary metastases from various specific tumors.

This book suffers from one major flaw, and that is the overall quality of the translations. In some chapters the translation problem is mildly amusing (such as the chapter on surgery of pulmonary metastases, where the innominate vein is consistently referred to as the anonymous vein) but does not represent a serious obstacle. In other sections the erratic translations make the message unintelligible except to the very experienced reader. Consequently, this is not a book I can recommend to medical students or residents. Although there is useful information contained, it can only be extracted by the experienced reader.

The final section of the book, which deals with the problem of metastases from specific tumors, is by far the strength of the book. In each of these chapters the pros and cons of surgical therapy are well laid out and thoughtfully explored. No unjustified claims for surgery are made and a thoracic surgeon reading these chapters will come away with a proper understanding of the role of surgery for lung metastases of various tumor origins. This is the perspective that is required to make appropriate decisions about the propriety of metastatectomy in a particular patient.

In sum, this is a book that would reasonably be available within the library of a division of thoracic surgery or department of surgery. It is recommended for any thoracic surgeon who wants to gain an overview of this problem in one sitting, which is possible as the entire book can be read in a relatively short time and the final section can easily be read in an hour or two. I cannot recommend this book for medical students or general surgery residents for the reasons given previously.

Las Vegas, Nevada

Use of a Total Wash-Out Method in an Open Heart Operation

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Pathological cold agglutinins may induce hemolysis in patients who need hypothermic cardiopulmonary bypass and blood transfusion. A simple technique, termed the total wash-out method, was used in a patient with high thermal amplitude, moderate-titer cold agglutinin before hypothermic cardiopulmonary bypass. The patient's cold agglutinin titer decreased abruptly after operation. None of the preoperative hemolysis phenomena were found during her 6 months of follow-up.

(Ann Thorac Surg 1989;47:57–8)

Cold agglutinins consist of monoclonal cold agglutinins and polyclonal cold agglutinins. Most monoclonal cold agglutinins are found in patients with lymphoreticular neoplasms. Polyclonal cold agglutinins are usually observed in association with infection, particularly mycoplasma pneumonia and infectious mononucleosis [1]. The clinical importance of cold agglutinins is the production of hemolysis or intravascular occlusive crisis when they are exposed to hypothermic conditions. This report describes a case of cold agglutinins that were probably caused by cytomegalovirus infection. The patient had a congenital ventricular septal defect and needed an open heart operation with hypothermia for cardiopulmonary bypass (CPB). Hemolysis was successfully prevented by using the total wash-out method before hypothermic CPB was instituted.

An 8-year-old girl (body weight, 20 kg) with acyanotic congenital heart disease showed a perimembranous ventricular septal defect with ventricular left-to-right shunt on cardiac catheterization. The shunting (pulmonary blood flow/systemic blood flow) was 2.2. There was a large interventricular septal aneurysm. The main pulmonary pressures were 36 mm Hg systolic pressure and 24.5 mm Hg mean pressure.

During preparation for surgical correction with CPB, anti-I antibody was found in her serum, which agglutinated all adult O^+ cells, but not cord cells. The antibody showed high thermal amplitude, and reacted even at 37°C. The patient's Coombs test was negative, including tests using broad spectrum, anti-immunoglobulin G, and anticomplement reagents. The cold hemagglutinin titer was positive at 1:128. The mycoplasma pneumonia antibody titer was negative at 1:40. The cytomegalovirus antibody Y value showed mid-range positivity (0.73). The operation was postponed and monitoring of the patient's cold agglutinins was done every 2 months. Six months later, her anti-I antibody was still present and the cold agglutinin titer persisted at a high level. Although plasma exchange has been reported as an effective method of treating cold hemagglutinin disease [1], the risk of hemolysis was still high in the presence of high thermal amplitude cold agglutinins. The total wash-out method was used to perform an open heart operation with hypothermic CPB.

Surgical Technique

After induction of anesthesia, a median sternotomy was performed. An arterial cannula was introduced into the ascending aorta. Both caval veins were cannulated through the right atrium and the venous tubes were clamped. At that time the heart was beating, and 2000 mL of venous blood was drained in three minutes from both caval veins into a prepared empty bottle. The venous blood was discarded, and the CPB was not started. At the same time 700 mL of warm Ringer's solution was infused into the aortic root to wash out any retained intravascular blood. The patient's blood pressure dropped below 20 mm Hg during this period. After this procedure, the venous cannulas were connected to the extracorporeal circulation system, which was primed with 1500 mL of type O blood. The aortic clamp was applied, and the total bypass was started. The cold cardioplegic solution (4°C) was rapidly infused from the aortic root. Moderate hypothermia (30°C) was induced. The right ventriculotomy was made. The patient had a moderate-sized ventricular septal defect with aneurysmal formation that could be closed primarily. After this was done, the right ventriculotomy was closed. Air in the left side of the heart was vented, and the aortic clamp was removed. The defibrillator was applied and the heart returned to normal sinus rhythm. The CPB was discontinued after 20 minutes of total bypass time. The patient was discharged after nine days in the hospital with an uneventful postoperative course. No hemolysis phenomenon was present during her 6 months of follow-up. The cold agglutinins showed a negative titer on the fifth postoperative day (1:4) and 1 month postoperatively (1:8).

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Comment

Low-titer immunoglobulin anti-I autoantibody is detected in the serum of healthy adults and infants [1]. The cold agglutinins are present in almost all normal subjects but are active as an autoantibody in vitro only [2].

Thermal amplitude and titer are the most important features of cold agglutinins as regards clinical symptoms of hemolysis or intravascular crisis. Wertlake and colleagues [3] reported a case of a patient with cold agglutinins who underwent a cardiac operation under hypothermia and developed persistent intravascular hemolysis for 1 week. Niejadlik and Lozner [4] found a patient with acute hemolytic anemia that was induced by a cooling mattress and a high titer of cold agglutinins secondary to mycoplasma pneumonia infection. Hemolysis is the major complication of cold agglutinins in patients who are exposed to hypothermia. Acute renal failure was noted by Carloss and Tavassoli [5]. Obviously physicians prevent these complications by not using hypothermia in patients with cold agglutinins.

If hypothermia cannot be avoided in these patients, some special techniques should be used to prevent the complications. Klein and colleagues [6] reported a case in which an 8-L plasma exchange by continuous flow centrifugation was used preoperatively to remove the cold agglutinins and permit the patient to receive an aortic valve replacement under hypothermia. Berreklouw and colleagues [7] developed an unusual technique for providing myocardial protection using a cold cardioplegic solution during a coronary bypass operation in a patient who had cold agglutinins and hemolysis.

Another well-controlled study of the effect of hypothermic CPB on patients with low-titer (less than 1:32), low thermal amplitude, nonspecific cold agglutinins was reported by Moore and colleagues [8]. These authors concluded that hypothermic CPB can be performed on these patients without increasing the risk of a hemolytic or agglutination crisis, and that some hemolysis occurs in all patients (whether or not they have cold agglutinin antibody) during hypothermic CPB, especially during the rewarming phase.

The case reported here is different in that the cold agglutinins had a high thermal amplitude and moderate titer (1:128). Cold agglutinin is specific for anti-I antibody. In this case, the cold agglutinins might have been caused by cytomegalovirus infection. Because the result of cross-matching between the patient's blood and all available adult donor blood revealed agglutination and hemolysis even at 37°C, hypothermic CPB or blood transfusion was bound to have induced the complications of hemolysis and intravascular occlusive crisis. We drained all the patient's blood as soon as possible (within three minutes) before hypothermic CPB and total blood transfusion. At the same time, we perfused lactate Ringer's solution into the aorta to wash out the intravascular retained blood. With this simple technique, the fatal complications of pathological cold agglutinins were prevented in this patient who needed to undergo hypothermic CPB and blood transfusion.

We thank Chien-Feng Sun, MD, for his help in clinical pathology.

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Notice From the American Board of Thoracic Surgery

The part I (written) examination will be held at the Hyatt-Regency, Dallas/Fort Worth Airport, Dallas, TX, on January 21, 1990. The closing date for registration is August 1, 1989.

To be admissible for the part II (oral) examination, a candidate must have successfully completed the part I (written) examination.

A candidate applying for admission to the certifying examination must fulfill all the requirements of the board in force at the time the application is received.

Please address all communications to the American Board of Thoracic Surgery, One Rotary Center, Suite 803, Evanston, IL 60201.

A Technique for Spot Application of Fibrin Glue During Open Heart Operations

Raul Garcia-Rinaldi, MD, PhD, Pat Simmons, RN, Victor Salcedo, MD,
and Carol Howland, BA

West Houston Medical Center and The Houston Heart Institute, Houston, Texas

Several techniques have been described for preparing and applying fibrin glue to control surgical bleeding. However, these methods tend to be cumbersome, expensive, or messy. Furthermore, commercial kits have not been approved by the Food and Drug Administration because of the potential risk of hepatitis contamination. Therefore, we have devised a modified, simpler technique that enables the precise, pinpoint application of fibrin glue. The risk of hepatitis transmission is substantially reduced by using cryoprecipitate plasma instead of fibrinogen from pooled donors. This technique is especially well suited for anastomoses of small vessels or for sealing suture holes in nonporous grafts.

(Ann Thorac Surg 1989;47:59–61)

The use of fibrin glue to control bleeding has gained increasing popularity in the United States [1–6]. Because of its versatility, fibrin glue has been used to seal vascular prostheses [7], suture lines in polytetrafluoroethylene grafts [8], the thoracic duct [9], and bronchopleural fistulas [10]. It is particularly useful during open heart operation in heparinized patients [4]. Commercial kits [8, 11] to prepare fibrin glue are available in Europe and South America, but the Food and Drug Administration has not approved their use in the US because of the potential for hepatitis B transmission from pooled blood donation [6]. Although several papers [1–3, 6] have described procedures for the in-hospital preparation of fibrin glue, its cumbersome application may discourage its use [6].

Several surgeons have devised techniques to facilitate the delivery of fibrin glue. Rousou and colleagues [1] described a two-syringe technique to deliver fibrin glue to a specific site. This technique, although innovative, is cumbersome because it requires holding each syringe with a separate hand. Consequently, mixing of the cryoprecipitate plasma and thrombin is uneven and dispersed. Baker and associates [5] recently described a technique for spray application of fibrin glue during cardiac operations, using fibrinogen and thrombin. We found this technique to be excellent because it produces a thin, layered clot that covers large operative areas. In our opinion, its best application is in patients who undergo repeat cardiac procedures. Unfortunately, the technique has disadvantages that limit its use. Because two vials of thrombin are required, the technique is expensive. Like that of Rousou and colleagues [1], it is not specifically suited for anastomoses of small vessels such as the internal mammary artery or for sealing the holes of sutures in nonporous grafts such as polytetrafluoroethylene. The kits available in Europe [8, 11] that we have used can deliver a spot application of fibrin glue with a Duploject clip (Immuno AG, Vienna, Austria) but are expensive, cumbersome, and difficult to obtain. The Food and Drug Administration has prohibited their clinical use because the fibrinogen component from pooled blood donors could potentially transfer the hepatitis virus [6] or acquired immunodeficiency syndrome [12]. Besides, the amount of fibrin glue produced (1 mL) is so small as to make their use impractical.

It is for these reasons that we have modified some of the existing techniques to allow the pinpoint application of hospital-prepared fibrin glue. Our modified technique has yielded excellent results in more than 100 heparinized patients. Because we use single-donor cryoprecipitate plasma, which allows screening of individual units, we practically eliminate the risk of transmitting the hepatitis B virus. This paper describes the technique of delivery employed.

Material and Methods

Cryoprecipitate plasma, kept frozen in our blood bank in 25-mL aliquots, is warmed for rapid thawing and decanted from the blood bank into a small cup. Twenty milliliters are then drawn into the first syringe. Next, bovine thrombin, packaged in the Thrombostat kit (Parke-Davis, Morris Plains, NJ) in 20,000 units, is diluted with 20 mL of saline, prepared to the specific concentration (1,000 U/mL), and placed in a second pan. Calcium chloride, 500 mg, is added to the thrombin to catalyze binding with fibrinogen. Next, 20 mL of this solution are drawn into the second syringe. It is essential that both syringes contain the same amount of solution (20 mL) so that the surgeon can use one hand to apply the solutions in equal amounts.

Mixing of the cryoprecipitate plasma and thrombin must be not only precise, but also instantaneous. Mixing should not occur in a common chamber, however, because this can cause clotting of the delivery system. Instead, a double-lumen catheter (Arrow International, No. AK-16702, Reading, Pa) is cut to 10 cm so that the

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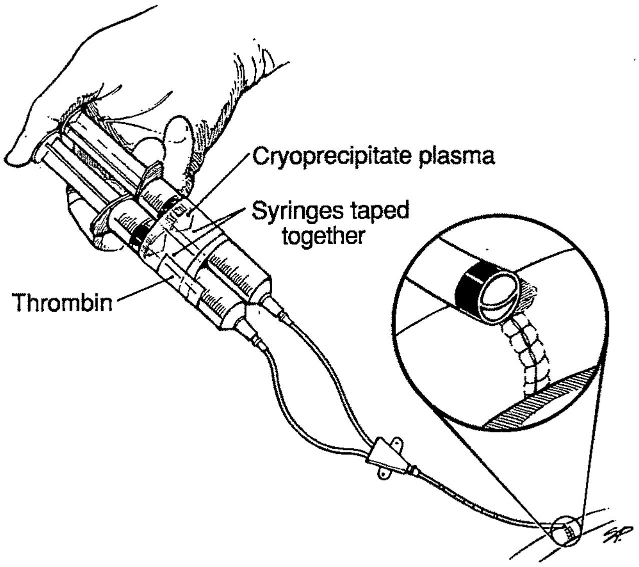

Fig 1. Two syringes, one with cryoprecipitate plasma (top), the other with the thrombin-calcium solution (bottom), are attached to the ports of the double-lumen catheter and taped together. The catheter is positioned directly over the area of application and the surgeon pushes the plungers of both syringes simultaneously with his thumb.

dual tract extends to the tip of the catheter (Fig 1, inset), and the two syringes are attached to the ports for injection and then taped together. A small "test clot" is formed in a pan or gauze sponge before application to ensure that the quantities and concentrations of the components will produce a firm clot.

The area that will receive glue should be as dry as possible to prevent washing away of the glue before full polymerization can occur. Although theoretically the thrombin is consumed, precautions should be taken to avoid disruption of hemostasis by the aspiration of free thrombin into the cardiopulmonary bypass circuit [11]. Therefore, the field is protected with a gauze sponge to prevent spillage [11]. The application of a gauze or Surgicel absorbable hemostat (Johnson & Johnson Patient Care Division, No. 1952, New Brunswick, NJ) over the area also serves as a matrix to allow polymerization and stabilization of the fibrin. To apply the glue in a 1:1 mixing ratio, the tip of the catheter is positioned directly over the area of application, and the plungers of both syringes are pushed simultaneously with the surgeon's thumb (Fig 1). Using this system of glue application, the surgeon can form a very small clot, such as required for an internal mammary anastomosis, or a larger clot to apply over an atriotomy or aortotomy. The clot forms within 10 seconds and enables rapid hemostasis.

Comment

We have observed with great interest the development of fibrin glue preparations available in Europe [7–9, 11]. These preparations are difficult to obtain, and the quantities of fibrin glue produced by these kits seldom exceed 1 mL. The spray application of Baker and associates [5] works very well in large oozing areas, such as in repeat cardiac operations. However, the method is expensive and does not allow the delivery of small quantities ("spot") of fibrin glue. Likewise, when we have tried the two-syringe delivery systems of Rousou and colleagues [1], they have yielded unequal, messy delivery of the cryoprecipitate plasma and the thrombin.

The technique that we have adapted achieves very thorough mixing of the two components at the delivery site and forms a firm clot. Increasing the thrombin concentration to 1,000 U/mL accelerates glue gelling [2] for rapid, reliable, and reproducible clotting. Because we use screened, single-donor cryoprecipitate plasma instead of pool-donated fibrinogen, the risk of transmitting hepatitis virus or acquired immunodeficiency syndrome is minimized. Alternatively, others have used the patient's own blood [13], fresh frozen plasma [2, 3], or stored human plasma screened individually for hepatitis B [6]. Using the patient's own blood, however, could deplete the patient, leading to transfusion, and requires planning that rules out emergency use. Fresh frozen plasma is expensive and does not meet "closed" system requirements for safe management of blood component products. Preparing fibrinogen concentrate from individual units of donor plasma by the blood bank methods of Spotnitz and colleagues [6] is safe, inexpensive, and effective, and provides a reasonable alternative to conventional cryoprecipitate. However, it does require prior preparation. We prefer cryoprecipitate plasma because it is readily accessible in the hospital and requires no prior preparation.

We encourage the use of this technique not only because it can help achieve hemostasis in small anastomoses, but also because it is cheaper and more versatile than the European products or the spray technique.

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REVIEW OF RECENT BOOKS

Guides to Clinical Aspiration Biopsy: Lung, Pleura, and Mediastinum

Liang-Che Tao
New York, Igaku-Shoin, 1988
497 pp, illustrated, $69.50

Reviewed by Thomas W. Shields, MD

A number of years ago, while a guest faculty member of the University of Toronto's thoracic surgical course, I had a discussion with one of the members of Toronto's faculty as to why at their institution they employed percutaneous transthoracic fine needle biopsy in all patients with peripheral lung lesions, as it is my own belief that this was unnecessary in most. He replied that it was because they were so good at it and had such a high diagnostic yield. After reading Dr Tao's book, I can understand his answer; their Cytopathology Department is not only good, it is excellent.

The author presents in a clear, concise manner the necessary techniques and precautions to obtain satisfactory cytologic smears for the interpretation of lesions within the chest. He then proceeds to describe in an understandable manner the cytopathological features of the benign and malignant processes, both primary and metastatic, that are encountered in the lungs, pleura, and mediastinum. The illustrations of both the aspirates and histological sections are superb. No one, of course, could become an "overnight" cytopathologist by using this book, but it provides the nonpathologist a basic understanding of what features the cytopathologist bases his diagnosis on. The author also nicely describes the use and value of the various immunocytological techniques that may be used to supplement, when indicated, the evaluation of the fine needle aspirates. He does point out, however, that such studies are inconclusive in 20% of the specimens studied.

The section on malignant lymphoma, particularly the discussion of the classification of non-Hodgkin's lymphoma, is especially illuminating. Unfortunately, new classifications appear with regularity but shed little light for better understanding of these diseases.

The author reports a false-negative rate of 6% with fine needle aspiration biopsies and emphasizes that clinical judgment is still an important ingredient in the management of patients with undiagnosed pulmonary, pleural, or mediastinal lesions.

The bibliography is extensive and up-to-date, and overall this is an excellent book; however, it is of somewhat limited value to the thoracic surgeon. Little fault can be recorded. One fault, however, is a possible misstatement that only 5% of patients who develop a postaspiration pneumothorax require a chest tube, an incidence of tube thoracotomy of less than 1.5% overall. In most clinics, the incidence is 25% of such patients for an overall incidence of 5% to 7%. Unfortunately, the author had no examples of nonseminomatous malignant germ cell tumors of the anterior mediastinum, and as a consequence no discussion of the important markers of these tumors was present.

These minor criticisms do not detract from the overall value of the book. Anyone interested in the cytomorphological identification of thoracic lesions should consider this text for his or her library.

Chicago, Illinois

Superior Vena Cava–Pulmonary Artery Shunt

William W. L. Glenn, MD

Charles W. Ohse Professor Emeritus, Department of Surgery, Yale University School of Medicine, New Haven, Connecticut

In 1954, because of the lack of consistently good results accompanying systemic artery–pulmonary artery shunting in certain patients with congenital cyanotic heart disease, my colleagues and I began experiments in our laboratory on shunting vena caval return to the pulmonary artery to partially or completely bypass the right side of the heart [1]. The physiologic basis of the procedure is that the low resistance to flow in the pulmonary circulation can be overcome by only a moderate increase in venous pressure while the principal function of the right side of the heart, delivery of venous blood at low pressure to the lungs, is maintained, although flow rate is reduced and ventricular pulsatility is absent. Studies conducted in our laboratory in 1948 to 1952 involving substitution of a mechanical pump for the right side of the heart [2] with diversion of the total caval return to one lung undoubtedly influenced our decision to attach the vena cava to the pulmonary artery directly to achieve a physiological bypass of the right heart. Because of our lack of scholarship, it was not until after our first clinical application of a superior vena cava (SVC)–right pulmonary artery (RPA) shunt that we were aware that in 1951 Carlon, Mondini, and DeMarchi had reported experiments with an SVC–RPA anastomosis [3]. A number of others were also investigating methods of bypassing the right heart in this same period.

In 1954 to 1958 we did over a hundred animal experiments on caval shunts with several configurations: SVC to RPA; inferior vena cava (IVC) to RPA, by partitioning a portion of the right atrial wall to the right pulmonary artery; and, together, SVC to left pulmonary artery (LPA) and IVC to RPA for total bypass of the right side of the heart, a procedure that gained no animal survivors. Although both SVC–RPA and IVC–RPA shunts were successful, the latter carried a high mortality and morbidity because of pooling of blood in the splanchnic area, and in a number of animals with the SVC shunt, chylothorax was produced (but was controllable) by ligation of the thoracic duct. The remarkable freedom from thrombosis in the SVC–RPA shunt (provided that needling of the vena cava, which produced a nidus for clot formation, had been avoided) and from constriction of the anastomosis, even after long survival of the animals, led us to believe the SVC–RPA shunt was safe for clinical application [4]. Our first clinical application was in 1958 to a 7-year-old child with transposition, single ventricle, and pulmonary stenosis (Fig 1, Fig 2) [5]. The patient today, 30 years later and after several additional operations to improve oxygenation of the venous return, is married and gainfully employed in an active business.

The conditions to be benefitted most by the shunt were soon defined. The two most common were tricuspid atresia and single ventricle with pulmonary stenosis. (At our institution there has been no operative mortality in 47 consecutive cases of SVC–RPA shunting for tricuspid atresia or single ventricle with pulmonary stenosis, despite the fact that many of the patients, most of whom were small children, were critically ill at the time of operation. Many of these operations were performed by Drs Gary Kopf, Hillel Laks, and H. C. Stansel.)

When it became obvious that the initial clinical improvement following the anastomosis was not being sustained, reasons for which were many, ways were introduced to further increase flow of desaturated venous blood to the lungs. Arterial shunts to the unshunted left pulmonary artery, if not already present, were established to provide additional palliation, for a while at least. An axillary artery–vein fistula was added to augment and enhance the flow through the SVC–RPA shunt [6].

The concept that after right atrium (RA)–pulmonary artery (PA) anastomosis, venous pressure alone or in combination with atrial contractions would provide the vis a tergo to move blood through the lungs was explored by Rodbard and Wagner [7] and Warden, DeWall, and Varco [8], but their experiments had limited success. Fontan and Baudet in 1971 [9] reported clinical application of an RA–PA shunt with additions and caveats. There were cogent arguments for and against the combining of this operation with an SVC–RPA shunt. Gradually, as experience was gained with the atriopulmonary procedure, it was modified to provide for specific lesions and to compensate for complications arising from performing it as originally described. Except for a few situations, there was abandonment of the SVC–RPA shunt, mainly because this shunt committed the larger right lung to oxygenating the lesser proportion of the venous return, ie, the return through the SVC. These exceptions were left ventricular failure with high left ventricular end-diastolic pressure, congestive heart failure due to overload of the right side of the heart, suitability of only one PA for venous shunt, and staging operation for children 6 to 24 months old, who had a normal-sized or enlarged PA.

In the meantime, modifications in the SVC–RPA shunt were made by several groups to include a redirection of caval blood to both right and left lungs by end-to-side SVC–PA anastomosis. Since 1967 Abrams has performed, with low mortality, bidirectional cavopulmonary shunts in 38 patients, among whom 6 had azygos continuity of the inferior vena cava (Abrams LD, personal communication, May 13, 1988). Kawashima and associates [10, 11] reported such shunts for azygos continuity of the inferior

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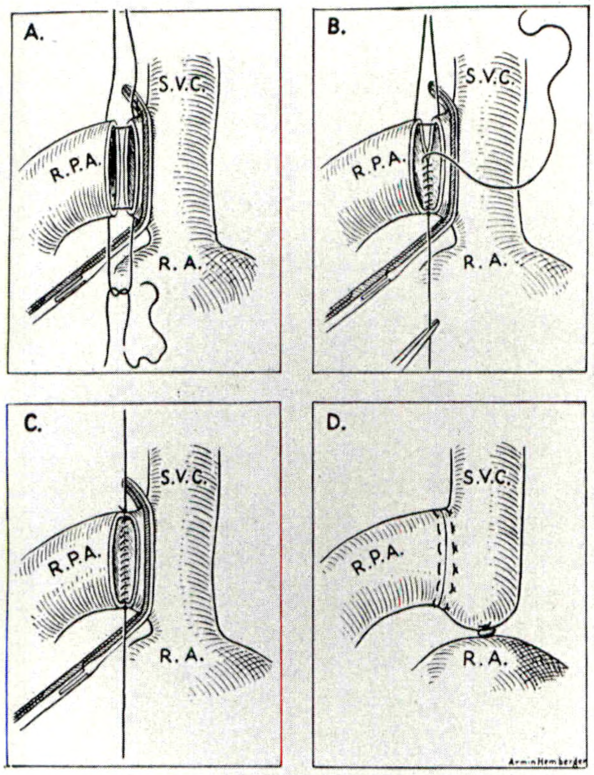

*Fig 1. Shunt between the superior vena cava and right pulmonary artery—technique of anastomosis. (*R.A. = *right atrium;* R.P.A. = *right pulmonary artery;* S.V.C. = *superior vena cava.) Reprinted by permission of the* New England Journal of Medicine *(1958;259:119).*

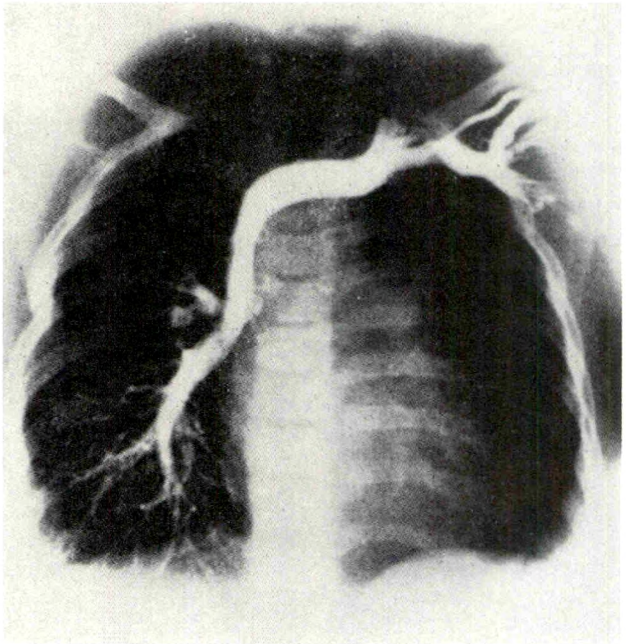

Fig 2. Angiogram taken 2 months after operation. Reprinted by permission of the New England Journal of Medicine *(1958;259:119).*

vena cava and other malformations. Hopkins and associates [12], in a comprehensive review including the physiological rationale for the bidirectional SVC–RPA shunt, reported making 21 such shunts, 14 of which were combined with atriopulmonary shunts. DeLeval and associates [13] were recently able to report making total cavopulmonary connections—bidirectional SVC–RPA and bidirectional IVC–main PA (accomplished by partitioning the RA).

In some patients with a venous shunt to one or both pulmonary arteries [11, 14, 15], normally occurring minute arteriovenous connections in the lung enlarge in the lower lobes, probably because of stagnation of flow, to become fistulous and cause precapillary shunting of blood and arterial desaturation. These fistulas increase in number with time and if clinically significant are obliterated by steel coil embolization [14, 15].

Thus, venous bypassing of the right side of the heart has been a changing tableau including many combinations of extracardiac and intracardiac rearrangements of venous connections to the PA. It is axiomatic, however, that the closer we come to mimicking the normal flow-pressure relationship in the PA that nature has provided for the right-sided circulation, the better the long-term results. It is not possible in right heart bypass procedures in *Homo sapiens erectus* to overcome the adverse effects of gravity on caval flow. These effects on inferior caval flow are minimized by relieving the RA overload by bidirectional SVC–RPA shunting. Alternatively the status quo of the IVC and RA is maintained and a bidirectional (or unidirectional) SVC–RPA shunt established, supplemented after a delay of several years by an axillary (or

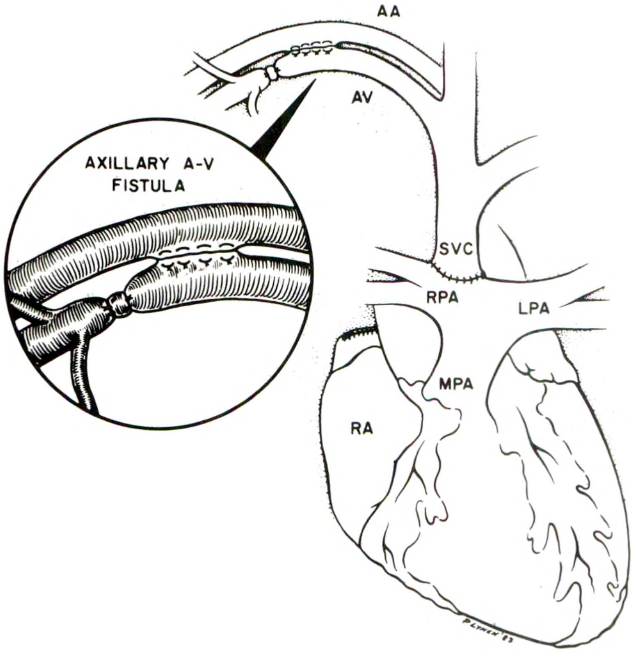

Fig 3. Superior vena cava–bipulmonary anastomosis with supplemental axillary arteriovenous fistula (see Reference 15). The maximum length of the anastomosis is 6 mm. At the suggestion of George Trusler (personal communication) the axillary vein is ligated distal to the shunt to avoid or minimize edema of the upper extremity.

brachial) artery–vein fistula (Fig 3) [6, 13, 15]. If intracapillary fistulas in the lung exist they are closed, preferably before the axillary artery–vein fistula is made [14]. Mild cyanosis persists, but chronic congestion of the lower half of the body and RA overload is avoided; further, flow to the lungs, with at least some pulsatility, is increased [6]. (For obvious reasons the creation of an axillary artery–vein fistula is contraindicated in the presence of an RA–PA shunt.)

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Notice From the American Board of Thoracic Surgery

The American Board of Thoracic Surgery began its recertification process in 1984. Diplomates interested in participating in this examination should maintain a documented list of the cardiothoracic operations they performed during the year prior to application for recertification. They should also keep a record of their attendance at thoracic surgical meetings, and other continuing medical education activities, for the 2 years prior to application. A minimum of 100 hours of approved CME activity is required.

In place of a cognitive examination, candidates for recertification will be required to complete both the general thoracic and cardiac portions of the SESATS III syllabus (Self-Education/Self-Assessment in Thoracic Surgery). It is not necessary for candidates to purchase SESATS III booklets prior to applying for recertification. SESATS III booklets will be forwarded to candidates after their applications have been accepted.

Diplomates whose 10-year certificates will expire in 1991 may begin the recertification process in 1989. This new certificate will be dated 10 years from the time of expiration of the original certificate. Recertification is also open to any diplomate with an unlimited certificate and will in no way affect the validity of the original certificate.

The deadline for submission of applications is July 1, 1989. A recertification brochure outlining the rules and requirements for recertification in thoracic surgery is available upon request from the American Board of Thoracic Surgery, One Rotary Center, Suite 803, Evanston, IL 60201.

Endoscopy, Mediastinoscopy, and Thoracoscopy

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Bronchoscopy

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    The value and risk of transbronchial biopsy of patients who require continuous ventilation is described.
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18. Wimberly N, Faling LJ, Bartlett JG. A fiberoptic bronchoscopy technique to obtain uncontaminated lower airway secretions for bacterial culture. Am Rev Respir Dis 1979;119: 337.
    The problem with contamination of specimens obtained through instruments being passed through the oral pharynx is solved by the use of shielded brush catheters as described.

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    A review of a large series of patients with primary pulmonary carcinoma demonstrating conclusively that the finding of malignancy in a stem bronchus is a significant prognosticator of survival.

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    A superb description of open tube and flexible bronchoscopy methods along with endoscopic pictures in color of normal and abnormal anatomical findings.

23. Taylor FH, Evangelist FA, Barham BF. The flexible fiberoptic bronchoscope: diagnostic tool or medical toy? Ann Thorac Surg 1980;29:546.

    A description of the use of the flexible fiberoptic bronchoscope passed through the open tube bronchoscope for accurate definition of pulmonary disease.

Laser Bronchoscopy

1. Dumon JF, Shapshay S, et al. Principles for safety in application of neodymium-YAG laser in bronchology. Chest 1984;86: 163.

    This paper describes the problems that can be encountered in using laser instruments and the methods used to avoid problems. The report comes from two busy laser endoscopic services in Marseille, France, and Burlington, Massachusetts.

2. Kvale PA, Eichenhorn MS, Radke JR, et al. YAG laser photoresection of lesions obstructing the central airways. Chest 1985;87:3.

    This recent description of the effects of neodymium yttrium-aluminum-garnet lasers on the obstructing lesions of the central airway reinforces what others such as McDougall at the Mayo Clinic, Dumon in Marseille, and Toty in Paris have described.

3. McElvein RB, Zorn GL. Indications, results and complications of bronchoscopic carbon dioxide laser therapy. Ann Surg 1984; 199:522.

    The carbon dioxide laser is useful for obstructing lesions and this report details the indications, results, and complications encountered using this modality.

4. Wolfe WG, Sabiston DC. Management of benign and malignant lesions of the trachea and bronchi with the neodymium-yttrium-aluminum-garnet laser. J Thorac Cardiovasc Surg 1986;91:40–5.

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Photodynamic Therapy

1. Cortese DA, Kinsey JH, Woolner LB, et al. Clinical application of a new endoscopic technique for detection of in situ bronchial carcinoma. Mayo Clin Proc 1979;54:635.

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4. Kato H, Konaka C, Ono J, et al. Preoperative laser photodynamic therapy in combination with operation in lung cancer. J Thorac Cardiovasc Surg 1985;90:420.

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5. McCaughan JS, Williams TE, Bethel BH. Palliation of esophageal malignancy with photodynamic therapy. Ann Thorac Surg 1985;40:113.

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Esophagoscopy

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    A discussion of the indications and contraindications of esophagoscopy and the complications of esophagoscopy and esophageal disease. The endoscopic findings in the normal situation and in a variety of diseases are described. The low incidence of complications is detailed.

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    A randomized controlled study that describes the application of the yttrium-aluminum-garnet laser to esophageal varices, demonstrating that the technique can control bleeding with fewer hospital deaths.

3. Giardet RE, Randall HT, Wheat MW. Palliative intubation in the management of esophageal carcinoma. Ann Thorac Surg 1974;18:417.

    A comprehensive review of the myriad of types of tubes available along with a discussion of methods of introduction and results.

4. Hirschowitz BI, Curtiss LE, Peters CW, et al. Demonstration of a new gastroscopy—the fiberscope. Gastroenterology 1958;35:50.

    The initial description of the flexible fiber endoscope, which revolutionized the field of gastrointestinal endoscopy.

5. Jones DB, Davies PS, Smith PM. Endoscopic insertion of palliative oesophageal tubes in oesophagogastric neoplasms. Br J Surg 1981;68:197.

    A description of esophageal dilatation and placement of an esophageal stent that has proved successful.

6. Keshishian JM, Smyth NPD, Maxwell DD, Chua L. Dilatation of difficult strictures of the esophagus. Surg Gynecol Obstet 1984;158:81.

    Stricture of the esophagus remains a problem, and this report describes a method of dilatation with a rigid endoscope and metal olive dilators.

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8. Olsen AM. Esophagology: an update. Ann Otol Rhinol Laryngol 1982;91:551.

   An overview by a senior endoscopist describing the instrumentation and indications in a number of esophageal disorders.
9. Sarr MG, Pemberton JH, Payne SP. Management of instrumental perforations of the esophagus. J Thorac Cardiovasc Surg 1982;84:211.

   Perforation of the esophagus is a catastrophic event, and this report details the management of perforations occurring in the cervical, mid, and distal esophagus with data demonstrating that most instrumental perforations of the esophagus should be managed surgically.
10. Soderlund C, Ihre T. Endoscopic sclerotherapy versus conservative management of bleeding oesophageal varices. Acta Chir Scand 1985;151:449.

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    A recent review of foreign bodies with a discussion of the relative merits of the rigid versus the flexible instrument.
12. Wolff WW. Current problems in surgery. Chicago: Year Book Medical Publishers, 1985;22:1.

    An excellent review of instrumentation and techniques available including sclerotherapy and laser therapy. Dilatation of the esophagus and the placement of prosthetic tubes are well described, as is the management of esophageal bleeding.

Mediastinoscopy

1. Ashraf MH, Milsom PL, Walesby RK. Selection by mediastinoscopy and long-term survival in bronchial carcinoma. Ann Thorac Surg 1980;30:208.

   A large experience demonstrating that mediastinoscopy can raise the resectability rate. The accompanying editorial by Pearson (p 205) must be read to clarify the management of patients who have positive mediastinal lymph nodes and who are resected with adjuvant therapy.
2. Carlens E. Mediastinoscopy: a method of inspection and tissue biopsy in the superior mediastinum. Dis Chest 1959;36:343.

   The initial description of mediastinoscopy such as is carried out today.
3. Foster ED, Munro DD, Dobell ARC. Mediastinoscopy: a review of anatomical relationships and complications. Ann Thorac Surg 1972;13:273.

   A seminal paper describing in detail the origin of mediastinoscopy, anatomy, complications, and observations regarding the results of mediastinoscopy.
4. Harken DE, Black H, Clauss R. A simple cervicomediastinal exploration for tissue diagnosis of intrathoracic disease. N Engl J Med 1954;251:1041.

   An interesting report that bridges the time sequence from a description of scalene node biopsy by Daniels to the subsequent description by Carlens of the techniques now used. The report reinforces the idea that mediastinal lymphadenopathy can be used for diagnosis and staging of intrathoracic disease.
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   This report from the Rutgers group, which has extensive experience in mediastinoscopy, demonstrates the feasibility of performing this operation in patients with superior vena cava obstruction.
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Thoracoscopy

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2. Dijkman JH, van der Meer JWM, Bakker W, et al. Transpleural lung biopsy by the thoracoscopic route in patients with diffuse interstitial pulmonary disease. Chest 1982;82:76.

   Another indication for thoracoscopy is described for establishing a diagnosis in 81 patients with diffuse pulmonary disease.
3. Miller JI, Hatcher CR. Thoracoscopy: a useful tool in the diagnosis of thoracic disease. Ann Thorac Surg 1978;26:68.

   A review of one year's experience at Emory University demonstrating the usefulness of this technique.
4. Oakes DD, Sherck JP, Brodsky JB, et al. Therapeutic thoracoscopy. J Thorac Cardiovasc Surg 1984;87:269.

   Thoracoscopy is described for therapy as well as diagnosis in a series of 13 patients, including removal of foreign bodies and institution of chemical pleurodesis.
5. Weissberg D, Kaufman M. Diagnostic and therapeutic pleuroscopy. Chest 1980;78:732.

   An extensive experience in 127 patients from Israel demonstrating results in both diagnosis and treatment of pleural disease.

THE SOCIETY OF THORACIC SURGEONS, THE AMERICAN ASSOCIATION FOR THORACIC SURGERY, THE WESTERN THORACIC SURGICAL ASSOCIATION, AND THE SOUTHERN THORACIC SURGICAL ASSOCIATION

TESTIMONY

George Miller, MD
Sacramento, California

before the
PHYSICIANS' PAYMENT REVIEW COMMISSION
November 2, 1988

I. Introduction

I am Dr. George Miller. I recently retired after having specialized in thoracic and cardiovascular surgery in Sacramento for 20 years. With me today are Dr. Sidney Levitsky, Professor of Thoracic and Cardiovascular Surgery at the University of Illinois, and Dr. Thomas Bartley from Pueblo, Colorado, former Professor of Thoracic and Cardiovascular Surgery and Dean of Continuing Medical Education at the University of Florida at Gainesville. Both are currently in active practice as surgeons and will help to answer any questions you may have.

We are here representing The Society of Thoracic Surgeons, the American Association for Thoracic Surgery, the Western Thoracic Surgical Association, and the Southern Thoracic Surgical Association. These are the four major thoracic and cardiovascular organizations in this country. Together, they represent virtually every thoracic and cardiovascular surgeon in the USA.

Since in Hsiao's RBRVS scheme intensity is a major component, I would like to offer a personal insight on intensity in our specialty. When I first began practice in a moderate-sized Kansas town, I essentially practiced as a general practitioner, then as a general surgeon. Finally, I trained and became board certified in thoracic and cardiovascular surgery and have practiced this specialty for over 20 years. I know the intensity level increased substantially when I went from family practice to general surgery, but the increase from general surgery to my present specialty was of a magnitude far greater than I imagined possible. Because of the ever-increasing technological advances, sicker and older patients, and greater patient expectations, that level of intensity has continued, if not increased, over the past decade.

II. Summary of Shortcomings Contained in Hsiao's Study

Although Hsiao has attempted a serious endeavor in trying to quantify the values of surgical and medical procedures, his studies contain a number of conceptual and methodological deficiencies which make it flawed and entirely unsuitable for setting payment policies or fee schedules at this time.

Over the past ten years, Hsiao's papers have attempted to develop a resource-based relative-value system (RBRVS), based on his perception that procedural services are overpaid compared to so-called cognitive services. We recognize that his present research differs technically, somewhat, from his 1985 research for the Commonwealth of Massachusetts.

Since both his 1985 and 1988 research had comparable objectives we would expect any differences in results would merely reflect improvements to the technical methodology he used in 1985. For this reason we would expect the relative values determined through his current research to have changed from those of his 1985 project only to the extent that the associated confidence intervals had narrowed.

However, if the 1988 results were substantially different from his 1985 results, then one must conclude that Hsiao's research is extremely sensitive to small changes in his assumptions, the selection and definition of resources, and the mathematical model. To our knowledge all of these decisions were made privately within Hsiao's research group with little or no significant external discussion.

Specifically, with regard to cardiac and thoracic surgical procedures, Hsiao's work contains many technical inaccuracies. These flaws affect the resulting RBRVSs and render the results wholly unreliable. Several of these flaws are:

A. The population sample selection techniques resulted in a biased sample;
B. The report does not demonstrate whether the high rate of non-respondents skewed the sample;
C. The increased time and intensity of modern procedures is ignored;
D. The overly simplistic methodology incorporates inaccurate assessments of the composition, time, and intensity of cardiac procedures;
E. The methodology of intensity and time calculations for high technology procedures is improper, skewing the results; and
F. The methodology for making intra-specialty extrapolations and cross-specialty linkages is flawed.

Each of these inaccuracies can distort the resulting RBRVSs, and reliance on those results could lead to policies which would work against the goals of the PPRC.

For these reasons, before Hsiao's work is considered as the basis of PPRC policies or proposed fee schedules, the shortcomings of his studies need to be carefully examined. At the present time the study should be judged as premature and unsuited for use in determining national health policies.

III. Discussion of Shortcomings

Hsiao's research has taken two and one-half years and has cost about $2,500,000. The "final" report of nearly 2,000 pages was delivered to the Health Care Financing Administration just 33 days ago, but copies were not available to our organizations until mid-October, 1988. Moreover, it appears that the "final" report is substantially incomplete.

Even at this late date, the Hsiao study omits extrapolations from the core groups of procedures to about 3,000 others. Also, the National Technical Information Service had technical problems in distributing Hsiao's data and results in machine-readable form until just a few days ago. In addition, we understand that the data and tapes for the extrapolated procedures will not be delivered to HCFA for another two months.

Thus, any real understanding of what the final report contains must be preliminary and limited. Nevertheless, we are continuing to study the released document as it relates to our specialty. As we learn more about the project's results, we will share it with PPRC.

As indicated earlier, our testimony focuses on several major deficiencies in the Hsiao report.

A. The population sample selection techniques resulted in a biased sample.

We note that the Hsiao project selected 100 thoracic and cardiovascular surgeons from the AMA list of self-proclaimed thoracic and cardiovascular surgeons. Hsiao explained in his March 1988 working papers (I, p. 22) that half of the thoracic and cardiovascular panelists were deliberately screened to consist only of general thoracic surgeons. Thus, the remainder were self-designated as thoracic and cardiovascular surgeons. We know from our recent national manpower survey that 30 percent of thoracic and cardiovascular surgeons do not perform cardiac surgery despite their titles; most of them do thoracic and vascular surgery. Since we also know Hsiao's telephone interviewers did not ask whether the respondents actually did cardiac surgery, it may be that considerably less than half of the respondents to the cardiac section of the Hsiao survey actually performed cardiac surgery. The Hsiao study did not have adequate quality control procedures to ensure that the surgeons actually do the procedures that they were queried about.

B. The report does not demonstrate whether the high rate of nonrespondents skewed the sample.

Hsiao had a high rate of non-respondents and did not characterize their practices. Were these doctors the busy, active, experienced surgeons who should have been interviewed? What were their practice patterns compared to the non-respondents in the survey? Although these two problems were repeatedly raised by the participants at the March 1988 consensus conference in Boston, to my knowledge they have not yet been answered.

C. The increased time and intensity of modern procedures is ignored.

No notice was taken of the recent significant advances in the coronary artery bypass procedure due to use of the internal mammary artery (IMA) as a bypass graft. The short and long-term results are far superior. Thus, the triple bypass using the autologous vein alone is being done less and less frequently. In statistics obtained from the Cleveland Foundation Clinic (over 1985–87), 77 percent of all coronary bypasses (5,687) used an internal mammary artery as one of the grafts. This, as we shall show later, increases the time and intensity of the operation. Thus, the procedure generally performed today is significantly different from the one examined by the Hsiao project.

At the same time, there is an increasing number of patients requiring repeat operations 1, 2, 10, or 15 years later due to the continued progress of the disease. These repeat operations are longer and more difficult due to scarring from the previous operation. The anatomy is harder to visualize resulting in greater risk of damage to the heart and great vessels. Thus, much longer time is required, in a more stressful situation. The Cleveland Foundation Clinic data show 19 percent of all cardiac operations were on patients who have had prior heart operations, and that percentage is consistent with national experience and is rising each year.

D. The overly simplistic methodology incorporates inaccurate assessments of the composition, time, and intensity of cardiac procedures.

From the interpretation presented by the Hsiao researchers, it appears they did not understand the technical sequences occurring during open heart surgery procedures. Thus, significant errors resulted in the data they collected.

For example, the estimated intra-operative time obtained from Hsiao's survey was skin-to-skin time (from the time of the incision until the dressing is placed on the wound). In cardio-thoracic surgery this skin-to-skin time is not appropriate. Our patients have an inherently unstable cardiovascular system—the one system that is especially vulnerable to developing problems when subject to the additional stresses of premedication, the insertion of monitoring lines, and general anesthesia. This pre-incision time is frequently the most intense of the total intra-operative period, since the circulation of the patient is subject to rapid deterioration.

The surgeon must be vigilant of the pressures and rhythm to detect downward trends and to reverse them, hopefully avoiding the need for an emergency opening of the chest. If the patient's condition does continue to deteriorate, we must splash on the antiseptic, manually pump on the chest while opening it, push in medications, and place the heart-lung machine conduits in and around the heart. All of these steps must be completed and circulation maintained so as not to go beyond the three to six minute time limit to keep the brain alive.

As a result of these conditions, we are actively and intensely involved in the care of the patient from the beginning of anesthesia until the patient's condition is stabilized in the cardiac recovery room. We believe that intra-operative time for cardio-thoracic surgery should be from the time the patient is placed on the table, the monitoring lines are placed, and anesthesia begins until the patient is in the cardiac recovery room (anesthesia time). Many hospitals require the surgeon to be in the operating room even earlier, when the patient arrives. This time is readily available from operating room records.

Hsiao found the mean operative time for triple coronary artery bypass to be 202 minutes. We felt this time did not reflect the actual operation's length. Smith, Bucklin and Associates, Inc., is conducting a survey of members of the Society of Thoracic Surgeons to obtain hard data from operating room records. A statistically significant number of responses have been received and those results show skin-to-skin times comparable to those used by Hsiao, and anesthesia times of 257 minutes using the autologous vein and 281 minutes using the vein and internal mammary artery. Thus, we believe operative time was underestimated by 79 minutes.

Clearly, Hsiao did not understand what occurs in the operating room. This problem is further magnified because he arbitrarily characterized time before the incision as merely pre-operative "wait-time", to which he assigned a value of one-half (1/2) that of the pre-service time. In fact, this pre-incision operative time is often more intense than the skin-to-skin time, and is far more intense than pre-service time. Pre-service time is very different. In pre-service time, the surgeon takes a history, talks to the family, and calls the referring physician. Relating pre-incision operative time to pre-service time is fundamentally incorrect.

Likewise, Hsiao misunderstands post-operative time. For most cardiac patients the early post-operative period is very hazardous because of the risk of bleeding, life threatening arrhythmias, respiratory problems, low urine output, low cardiac output, stroke, and cardiac arrest. This acute post-operative stabilization time must be given a higher level of intensity.

Hsiao relates post-operative intensity to the intensity of the intra-operative procedure, but in our field there are two distinct post-operative periods. The first period is this very intense post-operative stabilization period, and the second period is as characterized by Hsiao. The acute post-operative stabilization time is also spent in restoring adequate oxygenation, interpreting new chest x-rays and laboratory results, and, unfortunately, but not infrequently, returning urgently to the operating room for bleeding, cardiac arrest, tamponade, and other emergencies. Such returns to the operating room occur in about 5% of the patients.

This acute post-operative stabilization time varies from one patient to another—from a minimum of 60 minutes up to, not infrequently, 12 hours. At times, post-operative stabilization may require over 24 hours of nearly continuous active care of the highest intensity level.

E. The methodology of intensity and time calculations for high technology procedures is improper, skewing the results.

1. Mathematical transformations

By using mathematical transformations, Hsiao has distorted the time and intensity factors. First, in examining pre- and post-operative time and intensity, Hsiao inconsistently used a variety of different estimation techniques. In some cases different kinds of regression models were used, and in other cases "the clinical judgement of physician investigators" was used. Thus, Hsiao is constructing different RBRVSs using inconsistent methodologies.

Second, Hsiao makes a final adjustment to his "work" data through use of a modulating factor (Hsiao report, p. 480–485). This arbitrary adjustment using a four-level ordinal scale destroys the integrity of the data. Third, the intensity factors were subjected to logarithmic transformation, which causes the differences between low-intensity services (such as office visits) to be amplified and the differences between high-intensity services (such as the triple bypass) to be compressed.

The final result of these manipulations is to diminish the intensity of work artificially and arbitrarily for certain highly technical surgical procedures such as redo coronary artery bypass. Hsiao notes (p. 484) that "There is no objective standard with which we can compare our results to ascertain how well they represent reality." Furthermore, he notes that his pre- and post-operative services time estimation methodology and assumptions "raise the question of an imprecision or bias in our results."

2. Stress

The stress variable of work intensity is related to the anxiety induced in the physician exposed to personal, professional, and societal expectations for an excellent result following major technical surgery. While exacerbated by numerous clearly defined factors such as seriousness and severity of illness, uncertainty of diagnosis, and complexity of the case, there are other factors contributing to physician stress that are clearly related to the precision and technical demands inherent in cardiac surgery.

Operative mortality is an intense concern of the cardiothoracic surgeon with each patient. At the present time the only reliable non-vested mortality statistics concerning the results of cardiac surgery are available from the (1) New York State Registry, (2) VA Central Office Cardiac Surgeons Consultant Committee, and (3) DRG Hospital Mortalities compiled by HCFA. These sources indicate cardiac surgery mortality rates which are the highest of any surgical specialty.

Moreover, the fear of malpractice litigation for unsatisfactory results after the intense experience of surgical intervention in our specialty is difficult to measure, but

Table 1. Annual Malpractice Premiums

Specialty	Premium ($)
General practice	7,400
Cardiology (invasive)	11,640
General surgery	27,988
Cardiac surgery	41,776

Source: Illinois State Medical Society, 1988.

may be reflected, in part, by the ratio of the insurance premiums (Table 1). No other specialty of medicine has been subjected to a comparable level of public scrutiny and disclosure. For a variety of social, competitive, and political reasons, the media and the Government have scrutinized cardiac surgery results. The well publicized case of a single Naval surgeon has provided an additional source of psychological stress for every practicing cardiac surgeon.

F. The methodology for making intra-specialty extrapolations and cross-specialty linkages is flawed.

Despite the importance to his research project of extensions to procedures beyond the core group, we know Hsiao only asked each specialty panel about two dozen of its own procedures or services. Relative-value scales in the past have been developed by physicians knowledgeable in that specialty, who examined every included procedure or service. Hsiao has not yet reported his extension data. We question the accuracy of any extensions, particularly when the core data is seriously flawed, a core procedure is misunderstood, and the extension methodology is simplistic. We believe this aspect of the Hsiao research is defective.

With the Hsiao approach, there is an added problem in cross-linking specialties since the intra-specialty relative values are developed through different techniques. Attempts to cross-link such specialties using statistical comparative techniques obscures the different and often arbitrary underlying assumptions. It is like comparing apples and oranges. The results are at best meaningless.

IV. Medicare Part B Cost Reductions

PPRC now has before it an incomplete, unvalidated, and highly flawed survey for consideration regarding development of a national fee schedule and associated federal health policies. At best, all the Government can expect from a national fee schedule based on any relative-value scale is that it would be budget neutral and merely redistribute the available funds. It would not attack the problems of increasing volume and intensity. It would not save money.

Dr. William Roper, Administrator of HCFA, has asked the question, "Is it worth investing the lion's share of our analytic, administrative, and political resources to substitute one fee-for-service payment system for another, leaving Medicare's most important issue—increased volume and intensity—untouched?" (NEJM, September 29, 1988, p. 867).

But, it certainly would provide behavioral incentives. Wherever a RBRVS-based fee schedule was significantly in error, it would encourage the wrong behavior by the wrong physicians. The effect on access and quality of care could be profound. This damage would be unpredictable because no one knows where all the Hsiao RBRVS errors are or if, much less how, they could be corrected.

In fact, today every physician already has a Medicare fee schedule of his own, and no two are alike. We believe that distorted and inappropriate differences among these existing individual fee schedules should be reconciled. This task is manageable and the results would be predictable.

We believe that further consideration of the Hsiao approach is premature. Nevertheless, we want to work with PPRC in developing whatever reforms it decides to pursue.

We share PPRC's concerns about rising Part B health care costs. We believe that far greater savings can be realized in Part B of the Medicare program by concentrating on volume and intensity. Our specialty wants to be part of this process. We believe the following steps can be taken and significant savings will be realized:

1. Our society can develop guidelines to prevent overuse of medical and surgical modalities. Anti-trust considerations have prevented us from dealing effectively with this problem.
2. PPRC and HCFA can bundle services and procedures and can collapse CPT codes to control billing practices better. The Society of Thoracic Surgeons now has a recommended generic surgical bundle, and our representatives are working with PPRC in this area.
3. PPRC and HCFA can develop more effective ways of monitoring coding violations.
4. PPRC and HCFA can develop ways of discouraging the inappropriate use of consultants.

These approaches could save significant funds immediately without relying on an untested and flawed analysis of health care delivery and pricing policies, while preserving appropriate access to effective high quality health care for all Americans.

1988 Meeting Southern Thoracic Surgical Association

The Thirty-fifth Annual Meeting of the Southern Thoracic Surgical Association was held at Marriott's Marco Island Resort, Marco Island, FL, November 10–12, 1988. The President was O. B. Harrington, MD. Officers elected for the coming year are: *President*, Richard E. Clark, MD; *President/Elect*, Harvey W. Bender, Jr, MD; *Vice President*, William A. Cook, MD; and *Secretary-Treasurer*, Gordon F. Murray, MD.

The following 28 applicants were elected to membership:

Robert Anderson, MD
Palm Beach Gardens, FL

Michael J. Carmichael, MD
Gainesville, FL

W. Randolph Chitwood, Jr, MD
Lexington, KY

William C. DeVries, MD
Louisville, KY

Emery W. Dilling, MD
Austin, TX

Fred H. Edwards, MD
Washington, DC

Richard S. Faro, MD
Palm Beach Gardens, FL

Alessandro Ferrero, MD
Orlando, FL

Andrew C. Fiore, MD
St. Louis, MO

Brian L. Ganzel, MD
Louisville, KY

Ted E. Garrett, MD
St. Louis, MO

W. Peter Graper, MD
Melboure, FL

Arthur Grimball, MD
Charleston, SC

Robert A. Gustafson, MD
Morgantown, WV

Dennis L. Havens, MD
Lexington, KY

Bobby J. Heath, MD
Jackson, MS

Clarke L. Henry, Jr, MD
Kansas City, MO

Brian W. Hummel, MD
Lakeland, FL

Robert M. Hunter, MD
Raleigh, NC

M. Vinayak Kamath, MD
Augusta, GA

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Hiroshi Toyohara, MD
Knoxville, TN

E. Taliaferro Warren, MD
Jackson, MS

James B. Williams, Jr, MD
Abilene, TX

J. James Zocco, MD
Richmond, VA

Joseph B. Zwischenberger, MD
Galveston, TX

Elevated to senior membership were: Milton V. Davis, MD, Robert P. Dobbie, Jr, MD, Thomas B. Ferguson, MD, Thomas O. Gentsch, MD, James P. Lester, MD, Graydon A. Long, MD, William S. Lyon, MD, Isaac V. Manly, MD, Charles T. Meadows, MD, David V. Pecora, MD, Harold C. Spear, MD, John W. Sullenberger, MD, Lucas N. Turk III, MD, Paul M. Walstad, MD, and Raymond R. Watson, MD.

The President's Award for the best scientific paper given at the 1987 meeting was presented to Jean-Nicolas Vauthey, MD, Don W. Berry, MD, James C. Gilmore, MD, Kirsten Sundgaard-Riise, MD, Noel L. Mills, MD, and John L. Ochsner, MD, for the paper "Left Ventricular Aneurysm Repair With Myocardial Revascularization: An Analysis of 246 Consecutive Cases Over 15 Years."

The 1989 meeting will be held at the Phoenician Golf and Tennis Resort, Scottsdale, AZ, November 9–11, 1989. Chairman of the Program Committee will be Bradley M. Rodgers, MD, and chairman of the Membership Committee will be Hooshang Bolooki, MD.

Gordon F. Murray, MD
Secretary-Treasurer
Southern Thoracic Surgical Association
111 East Wacker Drive
Chicago, IL 60601

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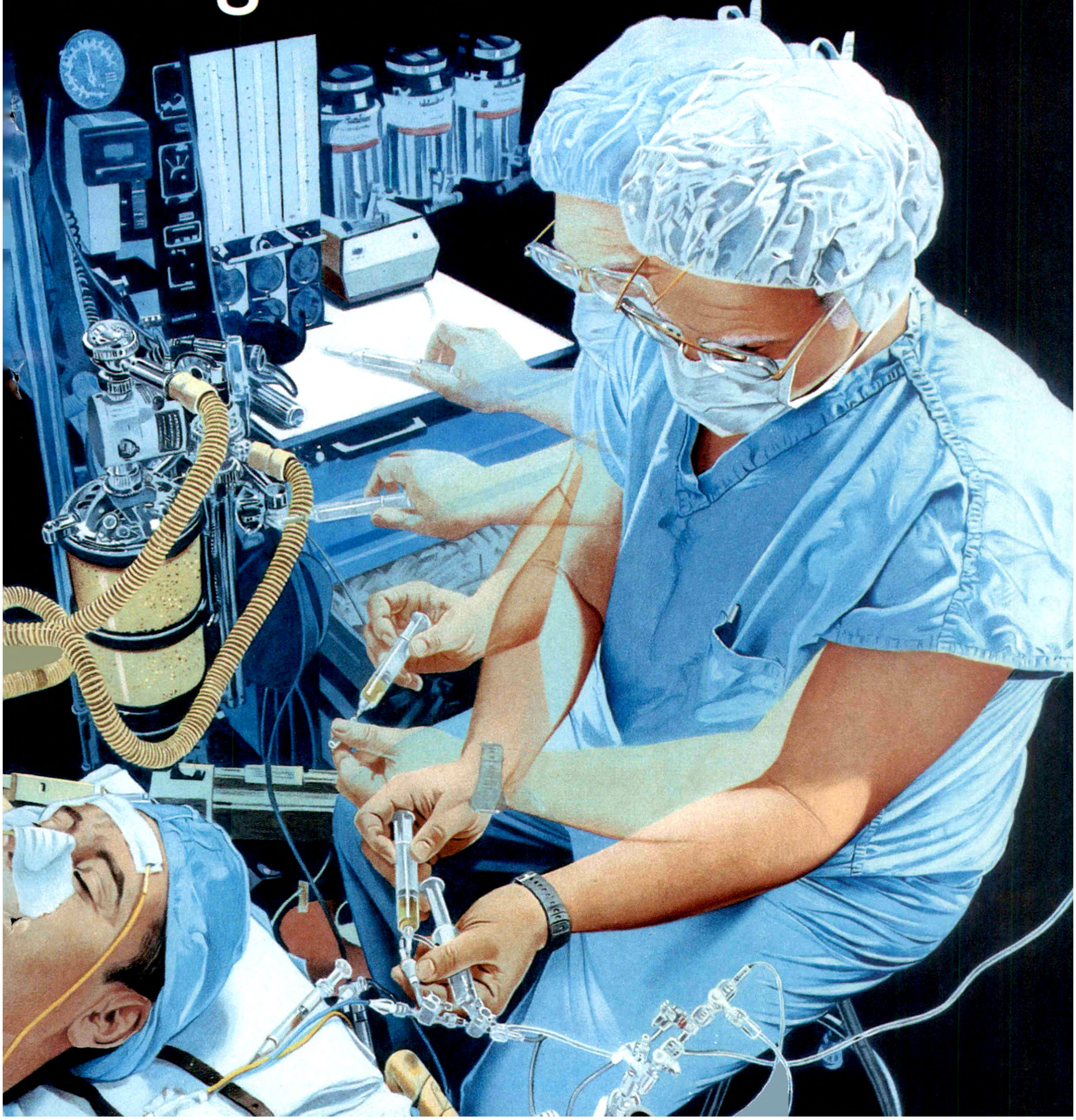
Ann Thorac Surg 1989;47:72 • 0003-4975/89/$3.50

Compromise[illegible] output, ischemia, and the highly vulnerable cardiac surgery patient…

The next crucial step: raising output without raising MVO_2



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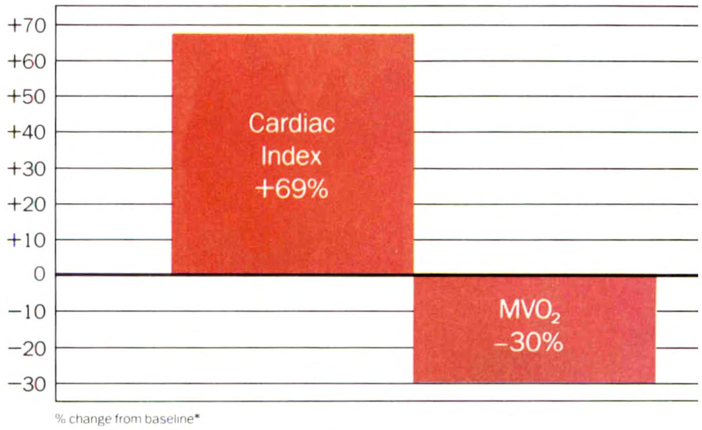
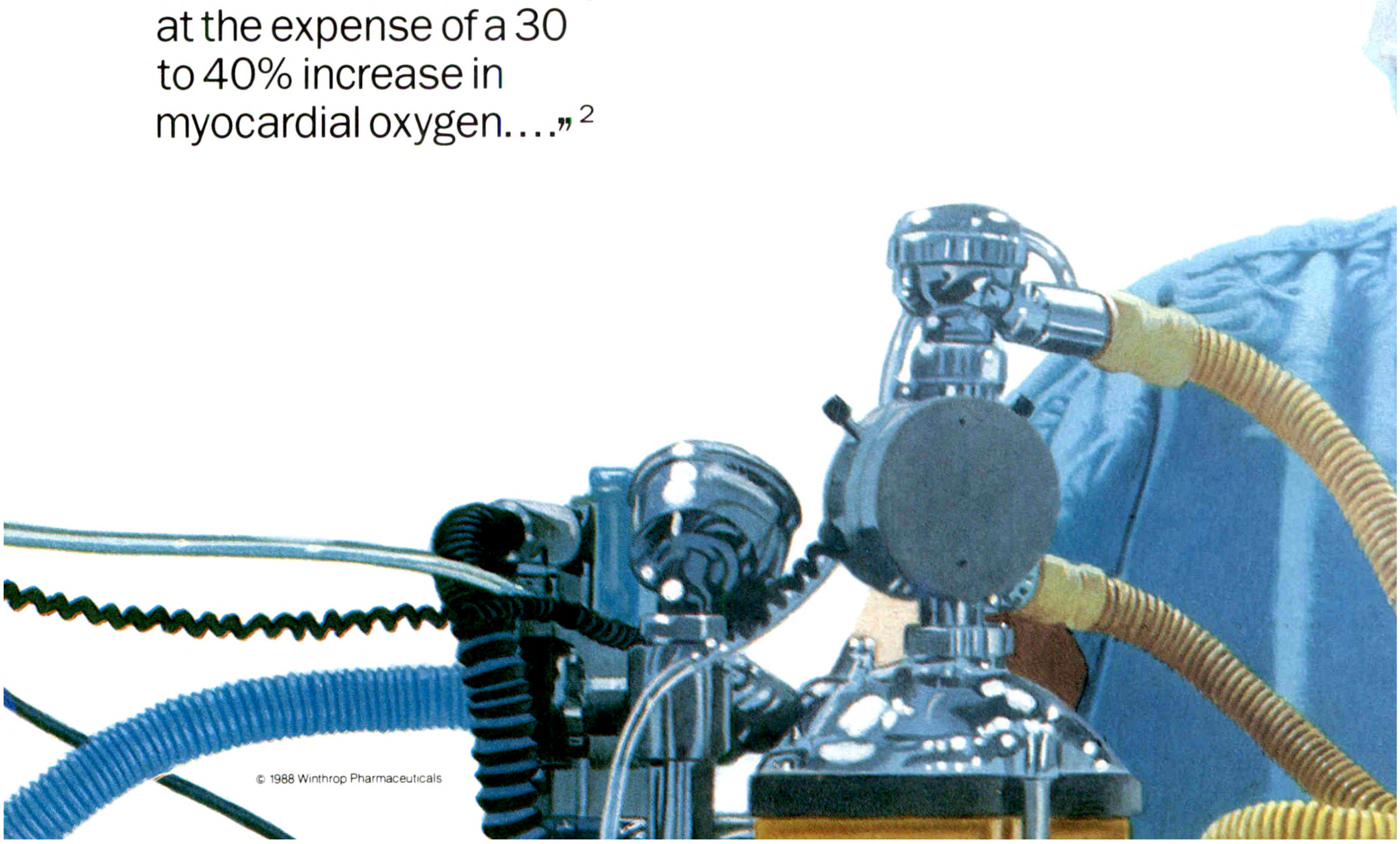
INOCOR I.V. (amrinone) provides improved hemodynamics without raising MVO_2 and worsening myocardial ischemia[1]



*n=8. Adapted from Benotti et al! Amrinone was infused in patients with severe congestive h
failure due to coronary artery disease at 2.5 mg/kg over 1 hour.

> "...hemodynamic improvements with catecholamine agents such as dobutamine tend to be achieved only at the expense of a 30 to 40% increase in myocardial oxygen...."[2]

1. Benotti JR, Grossman W, Braunwald E, et al: Effects of amrinone on myocardial energy metabolism and hemodynamics in patients with severe congestive heart failure due to coror artery disease. *Circulation* 1980;62:28–34.
2. Baim DS: Effects of amrinone on myocardial energetics in severe congestive heart failure. *Am J Cardiol* 1985;56:16B–18B.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- Unique mechanism of action—PDE III inhibition
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(AMRINONE)
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Please see following page for important product information concerning contraindications, warnings, adverse reactions, patient selection, and prescribing and precautionary recommendations.

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Brief Summary

Please consult full product information before prescribing. A summary follows. INOCOR lactate injection, brand of amrinone lactate, represents a new class of cardiac inotropic agents with vasodilator activity, distinct from digitalis glycosides or catecholamines.

INDICATIONS AND USAGE INOCOR lactate injection is indicated for the short-term management of congestive heart failure. Because of limited experience and potential for serious adverse effects (see ADVERSE REACTIONS), INOCOR should be used only in patients who can be closely monitored and who have not responded adequately to digitalis, diuretics, and/or vasodilators. Although most patients have been studied hemodynamically for periods only up to 24 hours, some patients were studied for longer periods and demonstrated consistent hemodynamic and clinical effects. The duration of therapy should depend on patient responsiveness.

CONTRAINDICATIONS INOCOR lactate injection is contraindicated in patients who are hypersensitive to it. It is also contraindicated in those patients known to be hypersensitive to bisulfites.

PRECAUTIONS *General:* INOCOR lactate injection should not be used in patients with severe aortic or pulmonic valvular disease in lieu of surgical relief of the obstruction. Like other inotropic agents, it may aggravate outflow tract obstruction in hypertrophic subaortic stenosis.

During intravenous therapy with INOCOR lactate injection, blood pressure and heart rate should be monitored and the rate of infusion slowed or stopped in patients showing excessive decreases in blood pressure.

Patients who have received vigorous diuretic therapy may have insufficient cardiac filling pressure to respond adequately to INOCOR lactate injection, in which case cautious liberalization of fluid and electrolyte intake may be indicated.

Supraventricular and ventricular arrhythmias have been observed in the very high-risk population treated. While amrinone per se has not been shown to be arrhythmogenic, the potential for arrhythmia, present in congestive heart failure itself, may be increased by any drug or combination of drugs.

Thrombocytopenia and hepatotoxicity have been noted (see ADVERSE REACTIONS).

INOCOR is not recommended for use in acute myocardial infarction.

LABORATORY TESTS *Fluid and electrolytes:* Fluid and electrolyte changes and renal function should be carefully monitored during amrinone lactate therapy. Improvement in cardiac output with resultant diuresis may necessitate a reduction in the dose of diuretic. Potassium loss due to excessive diuresis may predispose digitalized patients to arrhythmias. Therefore, hypokalemia should be corrected by potassium supplementation in advance of or during amrinone use.

DRUG INTERACTIONS In a relatively limited experience, no untoward clinical manifestations have been observed in patients in whom INOCOR lactate injection was used concurrently with the following drugs: digitalis glycosides; lidocaine, quinidine; metoprolol, propranolol; hydralazine, prazosin; isosorbide dinitrate, nitroglycerine; chlorthalidone, ethacrynic acid, furosemide, hydrochlorothiazide, spironolactone; captopril; heparin, warfarin; potassium supplements; insulin; diazepam.

One case of excessive hypotension was reported when amrinone was used concurrently with disopyramide.

Until additional experience is available, concurrent administration with Norpace® (disopyramide) should be undertaken with caution.

CHEMICAL INTERACTIONS A chemical interaction occurs slowly over a 24-hour period when the intravenous solution of INOCOR lactate injection is mixed directly with dextrose (glucose)-containing solutions. **THEREFORE, INOCOR LACTATE INJECTION SHOULD NOT BE DILUTED WITH SOLUTIONS THAT CONTAIN DEXTROSE (GLUCOSE) PRIOR TO INJECTION.**

A chemical interaction occurs immediately, which is evidenced by the formation of a precipitate when furosemide is injected into an intravenous line of an infusion of amrinone. Therefore, furosemide should not be administered in intravenous lines containing amrinone.

USE IN PREGNANCY *Pregnancy category C:* There are no adequate and well-controlled studies in pregnant women. Amrinone should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

USE IN NURSING MOTHERS Caution should be exercised when amrinone is administered to nursing women, since it is not known whether it is excreted in human milk.

USE IN CHILDREN Safety and effectiveness in children have not been established.

ADVERSE REACTIONS *Thrombocytopenia:* Intravenous INOCOR lactate injection resulted in platelet count reductions to below 100,000/mm^3 or normal limits in 2.4% of patients.

Gastrointestinal effects: Gastrointestinal adverse reactions reported with INOCOR lactate injection during clinical use included nausea (1.7%), vomiting (0.9%), abdominal pain (0.4%), and anorexia (0.4%).

Cardiovascular effects: Cardiovascular adverse reactions reported with INOCOR lactate injection include arrhythmia (3%) and hypotension (1.3%).

Hepatic toxicity: In dogs, at IV doses between 9 mg/kg/day and 32 mg/kg/day, amrinone showed dose-related hepatotoxicity manifested either as enzyme elevation or hepatic cell necrosis or both. Hepatotoxicity has been observed in man following long-term oral dosing and has been observed, in a limited experience (0.2%), following IV administration of amrinone.

Hypersensitivity: There have been reports of several apparent hypersensitivity reactions in patients treated with oral amrinone for about two weeks. Signs and symptoms were variable but included pericarditis, pleuritis, and ascites (one case); myositis with interstitial shadowing on chest x-ray and elevated sedimentation rate (one case); and vasculitis with nodular pulmonary densities, hypoxemia, and jaundice (one case). The first patient died, not necessarily of the possible reaction, while the last two resolved with discontinuation of therapy. None of the cases were rechallenged, so attribution to amrinone is not certain, but possible hypersensitivity reactions should be considered in any patient maintained for a prolonged period on amrinone.

General: Additional adverse reactions observed in intravenous amrinone clinical studies include fever (0.9%), chest pain (0.2%), and burning at the site of injection (0.2%).

MANAGEMENT OF ADVERSE REACTIONS *Platelet count reductions:* Asymptomatic platelet count reduction (to less than 150,000/mm^3) may be reversed within one week of a decrease in drug dosage. Further, with no change in drug dosage, the count may stabilize at lower than predrug levels without any clinical sequelae. Predrug platelet counts and frequent platelet counts during therapy are recommended to assist in decisions regarding dosage modifications.

Should a platelet count less than 150,000/mm^3 occur, the following actions may be considered:

- Maintain total daily dose unchanged, since in some cases counts have either stabilized or returned to pretreatment levels.
- Decrease total daily dose.
- Discontinue amrinone if, in the clinical judgment of the physician, risk exceeds the potential benefit.

Gastrointestinal side effects: While gastrointestinal side effects were seen infrequently with IV therapy, should severe or debilitating ones occur, the physician may wish to reduce dosage or discontinue the drug based on the usual benefit-to-risk considerations.

Hepatic toxicity: In clinical experience to date with IV administration, hepatotoxicity has rarely been observed. If acute marked alterations in liver enzymes occur together with clinical symptoms, suggesting an idiosyncratic hypersensitivity reaction, amrinone therapy should be promptly discontinued.

If less than marked enzyme alterations occur without clinical symptoms, these nonspecific changes should be evaluated on an individual basis. The clinician may wish to continue amrinone, reduce dosage, or discontinue the drug based on the usual benefit-to-risk considerations.

OVERDOSAGE Doses of INOCOR lactate injection may produce hypotension because of its vasodilator effect. If this occurs, amrinone administration should be reduced or discontinued. No specific antidote is known, but general measures for circulatory support should be taken.

HOW SUPPLIED Ampuls of 20 mL sterile, clear yellow solution containing INOCOR 5 mg/mL, box of 5 (NDC 0024-0888-20). Each 1 mL contains INOCOR lactate equivalent to 5 mg base and 0.25 mg sodium metabisulfite in Water for Injection. The pH of INOCOR lactate injection is adjusted to a range of 3.2 to 4.0 with lactic acid or sodium hydroxide.

Protect INOCOR lactate ampuls from light. Ampul packaging is light resistant for protection during storage.

Store at room temperature.

NOTE: Parenteral drug products should be inspected visually and should not be used if particulate matter or discoloration is observed.

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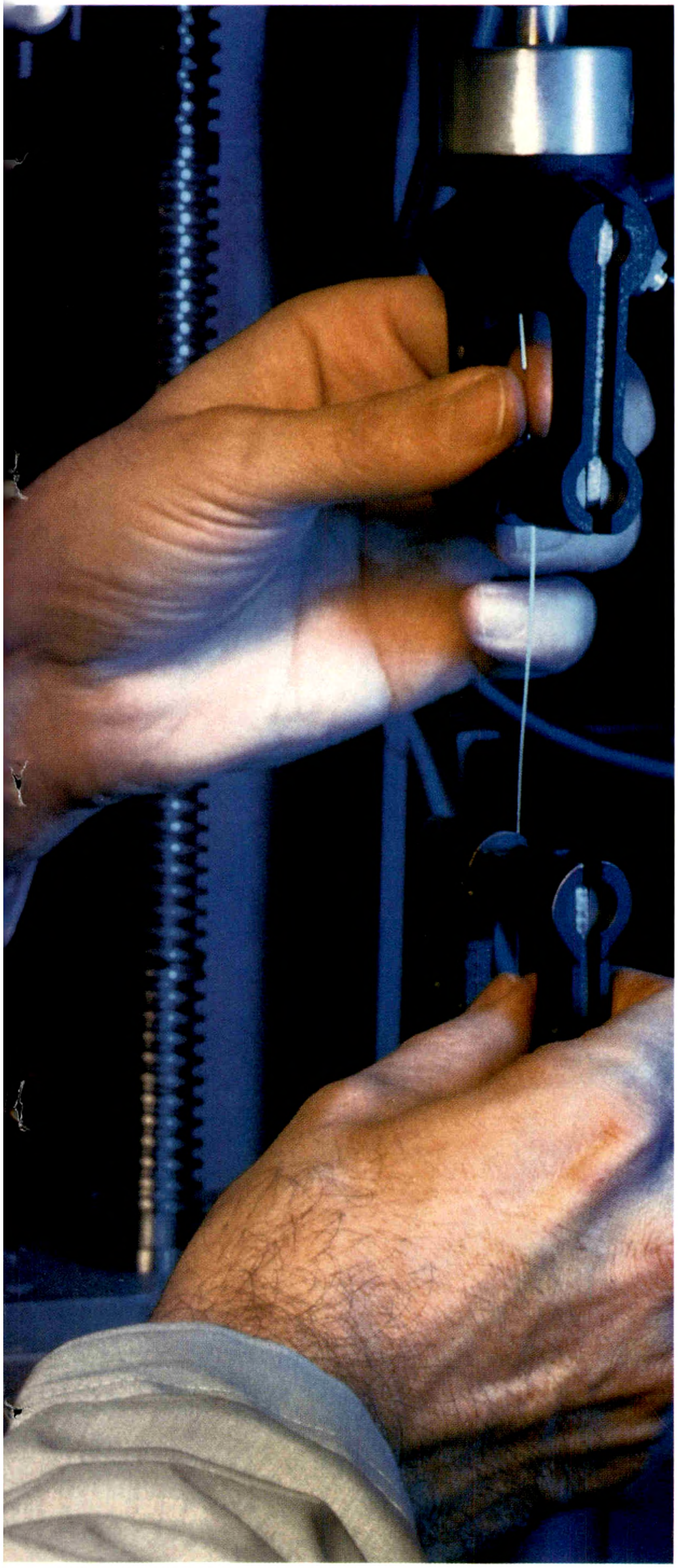

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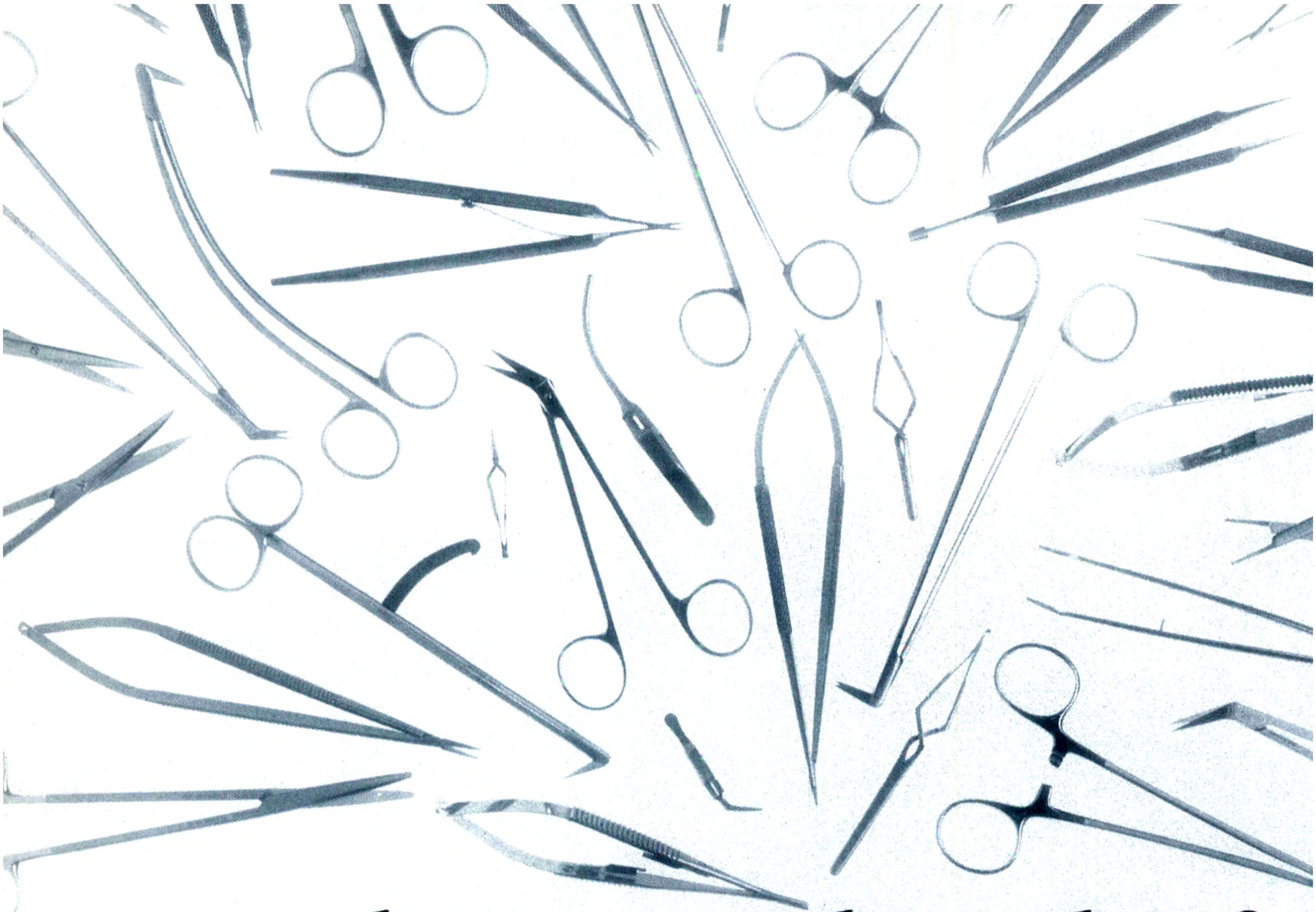

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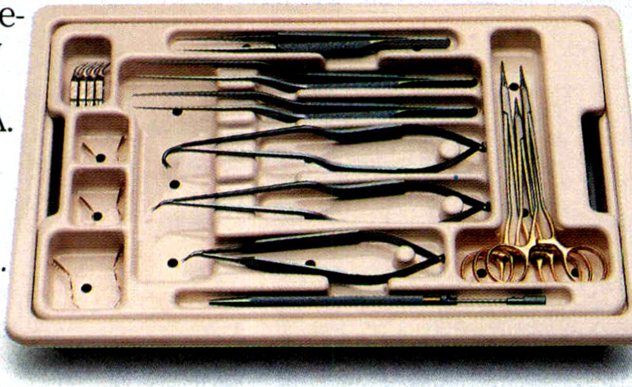

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Circulatory Support 1988

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Circulatory Support 1988

In April 1985, the Major Issues Committee of The Society of Thoracic Surgeons, chaired by George J. Magovern, recommended that the Executive Committee appoint an Ad Hoc Committee to Analyze Circulatory Assist Devices and Artificial Hearts. The committee's charge was to gather data, monitor legislation, evaluate the present status of the art, and indicate directions for the future.

In October 1985, President Albert Starr appointed the following committee members: D. Glenn Pennington (chairman), Jack G. Copeland, Charles Hahn, J. Donald Hill, George J. Magovern, Peer M. Portner, and Glenn Rahmoeller.

Since its inception, the committee has been active on behalf of The Society. As Chairman, I testified at the Food and Drug Administration hearings in Washington on the total artificial heart. In October 1986, we recommended that the Council approve monetary support for the petition of the American Society for Artificial Internal Organs to the FDA to ease restrictions on the development of new devices.

In April 1987, the Committee recommended that The Society sponsor a symposium on heart assist devices as a timely and important topic. The recommendation was endorsed by the Council, with the Ad Hoc Committee to act as the Program Committee. Although time was short, the symposium was set for February 1988, with St. Louis as the meeting site. Attendance was excellent, with 846 registrants (physicians, nurses, perfusionists, and engineers) from all over the world. There were 20 commercial exhibitors. Most of the papers and discussion given at the symposium are included in this special section of *The Annals*.

D. Glenn Pennington, MD
Chairman, Program Committee
Circulatory Support 1988

PROGRAM COMMITTEE

D. Glenn Pennington, MD, *Chairman*
St. Louis, MO

Jack G. Copeland III, MD, *Tucson, AZ*

Charles Hahn, MD, *Arzier, Switzerland*

J. Donald Hill, MD, *San Francisco, CA*

George J. Magovern, MD, *Pittsburgh, PA*

Peer M. Portner, PhD, *Oakland, CA*

M. Glenn A. Rahmoeller, *Silver Springs, MD*

Program

■ *Saturday, February 6, 1988*

7:40 AM **Welcome and Opening Announcements**
George C. Kaiser, MD
Problem Case Oriented Sessions With Panel Discussions

7:45 AM **1. Patient Selection***
Moderator: D. Glenn Pennington, MD
Panelists: Lyle D. Joyce, MD,
Walter E. Pae, Jr, MD, and
John A. Burkholder, MD

8:15 AM **2. Intraoperative Management***
Moderator: J. Donald Hill, MD
Panelists: Robert L. Hardesty, MD,
William A. Baumgartner, MD, and
Daniel M. Rose, MD

9:00 AM **3. Bleeding and Anticoagulation***
Moderator: Jack G. Copeland III, MD
Panelists: Laurence A. Harker, MD,
J. Heinrich Joist, MD, and
William C. DeVries, MD

9:45 AM **Break to Tour Exhibits and Posters**

10:30 AM **4. Other Postoperative Complications***
Moderator: William S. Pierce, MD
Panelists: Laman A. Gray, Jr, MD,
Lawrence R. McBride, MD, and
O. Howard Frazier, MD

11:15 AM **5. Weaning and Bridging***
Moderator: George J. Magovern, MD
Panelists: Leonard A. R. Golding, MD,
Philip E. Oyer, MD, and
Christian Cabrol, MD

12:00 noon **Luncheon**
Abhijit Acharya, PhD, Food and Drug Administration

1:15 PM **Videotape Session**
Moderator: Peer M. Portner, PhD

1. *Principles of the Bio-Medicus Centrifugal Pump and its Application to Circulatory Support*—Bio-Medicus, Inc
2. *Ventricular Assist With the Sarns Centrifugal Pump*—Sarns Inc/3M
3. *Emergency ECMO for Cardiopulmonary Support*—SciMed Life Systems, Inc
4. *Abiomed's BVS System 5000: Technical Principles and Clinical Application*—Abiomed, Inc
5. *Pulsatile Perfusion*—Elecath
6. *The Sarns Ventricular Assist Pump*—Sarns Inc/3M
7. *The Symbion Acute Ventricular Assist Device*—Symbion, Inc
8. *The Thoratec Pierce/Donachy Prosthetic Ventricle*—Thoratec Laboratories Corporation
9. *The Novacor Ventricular Assist System: Bridge to the Future*—Novacor Medical Corporation
10. *The Symbion Total Artificial Heart as a Bridge to Transplantation*—Symbion, Inc
11. *Surgical Implantation of the Heartmate Electrical Ventricular Assist System*—Thermedics, Inc

3:00 PM **Break to Tour Exhibits and Posters**

3:30 PM **Simultaneous Break Out Sessions**

Surgeons

3:30 PM **ECMO, Roller and Centrifugal Pumps**
Moderator: George J. Magovern, MD
Panelists: Kirk R. Kanter, MD,
Charles D. Campbell, MD,
Walter P. Dembitski, MD, and
R. Morton Bolman III, MD*

4:30 PM **External Pulsatile Pumps**
Moderator: William S. Pierce, MD
Panelists: Alain F. Carpentier, MD,
Jack G. Copeland III, MD, and
Laman A. Gray, Jr, MD*

5:30 PM **Internal Pulsatile Pumps**
Moderator: Peer M. Portner, PhD
Panelists: M. Arisan Ergin, MD,
O. Howard Frazier, MD,
Bartley P. Griffith, MD, and
Jacob Kolff, MD

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*This presentation is published in this special section.

Engineers/Perfusionists

3:30 PM **Internal Pulsatile Pumps**
Moderator: Harvey S. Borovetz
Panelists: Richard Smith, Phillip J. Miller, Stephen R. Igo, and James Ramsey

4:30 PM **ECMO, Roller and Centrifugal Pumps**
Moderator: Angelo K. Iatridis
Panelists: Ian Rosenberg, Paul R. Braun, and Ray Ramirez

5:30 PM **External Pulsatile Pumps**
Moderator: David Farrar
Panelists: Gerson Rosenberg, Marilyn Cleavinger, David F. Termuhlen, and Jean-Pierre Brugger

Nurses

3:30 PM **External Pulsatile Pumps**
Moderator: Marc T. Swartz
Panelists: Mary A. Goss and Jill Russell

4:30 PM **Internal Pulsatile Pumps**
Moderator: Julie A. Shinn
Panelists: Jan Muirhead, Marilyn Hravnak, and Sharon M. Augustine

5:30 PM **ECMO, Roller and Centrifugal Pumps**
Moderator: Rosemary C. Gaglia
Panelists: Pam Sakert, Karen Caruana, Shelly A. Ruzevich, and Theresa Boley

6:30 PM **Cocktail Reception in Exhibit Hall**

■ *Sunday, February 7, 1988*

General Sessions With Invited Speakers (Systems and Results)
Moderators: George C. Kaiser, MD, and Robert L. Replogle, MD

7:30 AM **1. Cardiac Resuscitation With Percutaneous Groin Cannulation**
Steven J. Phillips, MD*

7:40 AM **2. Cardiac Resuscitation With ECMO**
Kirk R. Kanter, MD

7:50 AM **3. Cardiac Resuscitation With Left Atrial Cannulation**
Joseph M. Cunningham, Jr, MD

8:00 AM **Discussion**

8:15 AM **4. Postcardiotomy Support With Roller Pumps**
Daniel M. Rose, MD*

8:30 AM **5. Postcardiotomy Support With Centrifugal Pumps**
George J. Magovern, MD

8:45 AM **6. Postcardiotomy Support With Pulsatile Ventricular Assist Device**
D. Glenn Pennington, MD*

9:00 AM **Discussion**

9:15 AM **Break to Tour Exhibits and Posters**
Moderators: Denton A. Cooley, MD, and Jack G. Copeland III, MD

10:00 AM **7. SWAT Team Approach to Assist Devices**
Jean-Pierre Brugger, PhD*

10:15 AM **8. Implantable Electrical Left Ventricular Assist Devices**
Peer M. Portner, PhD*

10:30 AM **9. Bridging to Transplantation With Heterotopic Artificial Ventricles**
Alain F. Carpentier, MD

10:45 AM **Discussion**

11:00 AM **10. Bridging to Transplantation With the Jarvik-7 Total Artificial Heart**
Christian Cabrol, MD*

11:15 AM **11. Bridging to Transplantation With Artificial Hearts**
Bartley P. Griffith, MD*

11:30 AM **12. Summary of Bridging to Transplantation Experience**
J. Donald Hill, MD*

11:45 AM **Discussion**

12:00 noon **13. Report of Circulatory Support Registry**
Walter E. Pae, Jr, MD

12:15 PM **14. Experience With Permanent Artificial Hearts**
William C. DeVries, MD

12:30 PM **15. Devices of the Future**
William S. Pierce, MD*

12:45 PM **Discussion**

1:00 PM **Adjournment**

2:00 PM **Optional Session on Regulatory Issues**
Chaired by The Society of Thoracic Surgeons
Scientists from the Food and Drug Administration will be present. The session is intended to be an open forum for discussion of regulatory issues from the perspectives of clinicians, the FDA, and the industry.

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*This presentation is published in this special section.

Panel 1

Patient Selection

Moderator: D. Glenn Pennington, MD
Panelists: Lyle D. Joyce, MD, Walter E. Pae, Jr, MD, and John A. Burkholder, MD

MODERATOR PENNINGTON: Our first panel for this morning is to deal with the important question of patient selection. In my own mind patient selection in applying these devices is extremely important and perhaps the most important issue. I don't know that we know the answers, but at least we have some guidelines that we will be able to offer you.

The panelists are Dr John Burkholder from Allegheny Hospital in Pittsburgh, who has had extensive experience with the Bio-Medicus pump; Dr Walter Pae of Hershey-Penn State, who has a large experience with the Pierce–Donachy and the Penn State Artificial Heart; and Dr Lyle Joyce from Minneapolis, who has had experience with the Jarvik heart and the centrifugal pumps. So, we have most of the various disciplines represented.

I would submit this rather worn-out information (Table 1) to you as being still the criteria by which patients must be selected, that is, the definition of cardiogenic shock. After all, that is the group of patients we are concerned about in the application of virtually all these devices. The exact numbers, of course, are not so critical, but it is critical that we actually make the measurements. Cardiac output measurements in the operating room, for example, are absolutely essential to the use of these systems. One must measure the atrial pressures, and we believe it is absolutely essential that the left atrial pressure line be used, not a wedge pressure from a Swan catheter. All these measurements must be carefully made and repeated to be certain that they are accurate.

The definition of maximal inotropic support is one that might be debated long and hard, but most of us know that when we are in the polypharmacy and our anesthesiologist is at his wit's end with the patient still not making it, we have to offer more support. Almost all of our patients receive a balloon pump before the insertion of one of these devices. Whether these exact criteria would be agreeable to you or not is not important. The important thing is that the measurements be made and that some sort of systematic method be used to choose patients.

Probably one of the most important things not stated in this table concerning postcardiotomy patients is that we must be absolutely certain that the operation that we set out to do has been done appropriately and properly. These devices are definitely not to be used to cover up inadequate or inefficient operations. So we want to be sure that the patient has had an optimal operation.

Now, who should be excluded? The criteria we have adopted were somewhat difficult to come by, but these exclusions evolved from our experience with an NIH contract group in which four institutions studied the clinical application of these devices.

Of course, the body surface area depends on the type of device, and we will discuss that more later. The age, as far as I am concerned, is still somewhat negotiable. Renal failure has not been well defined, and we will deal with that in our discussions. Cerebrovascular disease, hepatic failure, and multiple organ failures are fairly well defined. Massive bleeding is sometimes difficult to predict. Active infection is also an issue that is sometimes difficult to determine. Despite these problems, these exclusion criteria were adhered to pretty carefully in our NIH study and generally were applicable.

I'm just going to entertain one quick thought about our own experience in dealing with postcardiotomy patients. We have looked carefully at 46 postcardiotomy patients supported with the Pierce–Donachy pump or some type of centrifugal pump. Retrospectively, we found that the occurrence of an acute perioperative myocardial infarction, that is, an infarction within 24 to 48 hours of operation, was a very important determinant of survival. Among 46 patients, we had 12 survivors and 34 nonsurvivors. Of the survivors, there was only 1 who we think had a definite perioperative infarction, whereas among nonsurvivors the incidence of perioperative infarction was 70%.

When we examined those infarcts at autopsy in the patients who did not survive, we found that the vast majority of them were biventricular; so, the incidence of biventricular failure in our patients was also relatively high. Currently we believe that a large or at least a clinically significant perioperative infarction with biventricular failure has a strong negative impact on survival. Others may not corroborate those findings, but in our experience that seems to be the case.

In essence, what we need to know in the operating room is how to separate out an infarcted ventricle from a stunned myocardium, but unfortunately, we don't know yet how to do that. Until we do know, we're still going to deal with this problem.

Next, I'd like to introduce our panelists, who will also give you a quick summary of a few issues, and then we will begin discussion.

The first summary will be by Dr John Burkholder, who will discuss the problem of multiple organ failure.

DR BURKHOLDER: Thank you, Glenn. It is a real pleasure to have the opportunity to discuss some of our experience from Allegheny General Hospital in Pittsburgh.

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Table 1. Criteria for Ventricular Assist Device Support

Cardiac index < 2.0 L/m^2/min
Systemic vascular resistance > 2100 dynes/s/cm^5
Atrial pressure > 20 mm Hg
Urine output < 20 mL/h with:
Optimal preload
Maximal drug therapy
Corrected metabolism
Intraaortic balloon pump

We have accumulated 59 patients who required postoperative left or right heart assist, or both, using in all cases the Bio-Medicus Vortex pump. Of these 59 patients, we had 21 long-term survivors. This population we define as those people who have survived in excess of 30 days. Short-term survivors were weaned but did not survive the requisite 30 days, and, of course, the nonsurvivors are self-explanatory.

Of the long-term survivors, we had 11 who had left heart assist only, 9 who had biventricular assist, and 1 who had right heart assist. The proportion in the nonsurvivors is amazingly similar; a total of 36 of the 59 patients had left heart assist only and 21 had biventricular assist. Of the long-term survivors, our longest survivor has lived in excess of 6 years. We have 12 known survivors, 6 known dead out of that population, and 3 patients whose status we could not determine just prior to this meeting.

Glenn asked me to look at determinants for survival or try to see whether or not organ failure other than heart failure can help us to select patients who will be good candidates for post-pump ventricular support. We defined renal failure as a clinically significant preoperative elevation in creatinine and blood urea nitrogen. In our population of 59 patients, we actually had only 1 patient out of the entire group who we could have classified as a preoperative renal failure. He fell into the nonsurvivor group. So, I really can't help you from the standpoint of whether or not this is a good indicator. I think we probably preselected the renal failure group out before we even thought of postoperative ventricular support.

Patients with impaired preoperative neurologic status were defined as patients who had a stroke by history but were relatively stable preoperatively or showed some signs of neurologic obtundation secondary to low cardiac output. The experience of the total number of patients is spread relatively evenly over the three groups and really doesn't add an awful lot of information regarding whether or not we can preselect survival patients based on neurologic status.

As Glenn has previously mentioned in his criteria, among patients who have chronic obstructive pulmonary disease, the data are skewed toward nonsurvivability if the preoperative obstructive lung disease is severe.

None of the patients that had preoperative hepatic dysfunction, frank jaundice, or elevated enzymes indicating an active liver process survived. We simply didn't have any experience with hepatic dysfunction in long-term or short-term survivors.

The status of the patients as they arrived in the operating room was most significant. That is, patients that come to the operating room in full cardiac arrest or in cardiogenic shock with balloon support or classified as an emergency, in other words, the "crashing" patients coming from whatever origin, uniformly do not do well. The stage is set for cardiac failure even before you have a chance to do your operation. In our experience, even after we had done everything that we could possibly do from a surgical standpoint, 7 out of a total of 11 patients were not weanable ultimately from postoperative heart assist, 4 of 11 were weaned but were short-term survivors, and none of these people survived 30 days after their operation.

MODERATOR PENNINGTON: Walter Pae now will discuss with us the choice of the patients in terms of their age, their size, and other measurements.

DR PAE: I have been given the relatively easy task of discussing patient selection on the basis of size and age. In terms of patient size, with the roller and centrifugal pump systems there really are not any limitations whatsoever. Limitations are based only on the ingenuity of the cardiac surgeon to adapt these readily available devices for postcardiotomy cardiogenic shock in the very small or large patient. However, the pneumatic pumps are clearly limited at the present time by the size and stroke volume of the devices and inlet and outlet cannula size as well as length. These devices cannot be used practically in patients weighing less than about 40 kg or with a body surface area of less than 1 m^2, and accordingly should probably not be applied in these patients. A problem can occur in the patient that is a bit large, again because of inlet cannula length, which may be too short to allow sufficient length for the tube to exit the skin subcostally.

In terms of patient age, probably the physiologic age is the most important consideration. However, if you do look at a large number of patients, there are certain generalizations, I think, that can be made in terms of patient selection.

According to data from the Combined Registry (ASAIO-ISHT) on approximately 318 patients supported with ventricular assist devices (VADs) for postcardiotomy cardiogenic shock, at the end of the age spectrum, survival is quite different than it is for the patients in the less than 65 years age groups. Application of ventricular assistance for postcardiotomy cardiogenic shock in patients above 65 years of age yields a survival of about 12% in the 66 to 70 years age group, and above 70 years of age a survival of only about 6%. This contrasts markedly with survival rates of 21% to 31% in patients less than 65 years of age. So I think the data can be summarized by simply saying that once one gets into the age range of 65 years and older there is a tremendous amount of concomitant disease and one might expect a poorer outcome.

MODERATOR PENNINGTON: Lyle Joyce now will discuss some of the intraoperative problems such as bleeding and coagulation disorders and how the presence of a preexisting infection might affect his selection.

DR JOYCE: Thank you, Glenn.

I have been asked to discuss some of the variables that affect survival with the use of VADs. Unfortunately, they are figures that are not easy to come by. We'll talk for a minute about preoperative infection and then the question of whether the original operation was a primary or a repeat operation, and then the importance of the length of the cardiopulmonary bypass run and the importance of coagulopathy.

In terms of infection, there is not a great experience with use of VADs (or total artificial hearts, for that matter) in the face of preoperative infection. More often than not these patients are individuals who have gone into the operating room electively or at least on an emergency basis in a hopefully noninfectious state; therefore most of the experience is anecdotal.

If we look at the registry that Dr Pae has collected, we actually can get figures that are a little bit confusing. In fact, weaned patients actually have had a greater incidence of infection on the device than the nonweaned patients. What does this tell us? Basically, it probably tells us that if we have any of today's devices in place for a long enough period of time, we will eventually get some type of infection, whether it is a septicemia or a positive culture of the mediastinal contents. The patients who die early and can't be weaned from the VAD support don't have time to get infected. It would only be expected that those patients who are weaned, and therefore have done better, will have a higher incidence of infection.

An extremely poor prognosis, however, exists if the infection persists once the device is removed. It appears from the anecdotal experiences that we can find throughout the country that just because the mediastinum might be positive at the time the device is removed does not necessarily spell disaster in the postremoval period. Perhaps the one place where this is not true is in the case of the total artificial heart, where we are going to the state of transplantation requiring immunosuppression.

Dr Bartley Griffith published his data back in the fall demonstrating that at least 5 of 6 patients who had mediastinitis before transplantation did not survive once the device was removed. There has been some survival in other centers, however, in patients who were transplanted after having a positive mediastinal culture.

Just a quick comment about the repeat versus primary operation. There are only a few cases of repeat operations associated with the use of VADs or total artificial hearts. It is something that the registry doesn't collect at the present time and there may be more out there than we know about. The ones that we are aware of do not seem to have any relationship between survival and whether it was a first or a second time operation. Basically, I think we all understand that a repeat operation is more prone to bleeding and we may spend more time in the operating room with that particular case, but the final outcome is not necessarily negative in a repeat operation.

If we look at the time that the patient was on bypass and try to correlate that with survival, we get all sorts of mixed figures. From the summary of our experience in Minnesota using the centrifugal pumps we can see that the patients who were unweanable from the pump were actually on the VAD longer than the other individuals. There seems to be no trend there whatsoever as far as the importance of length of time on the VAD in the short-term or long-term survivors. Dr Burkholder's data were a little bit different, skewed in the other direction, and I think every center that we look at sort of has mixed figures. It is interesting that the registry shows no survivors among patients who were on cardiopulmonary bypass for greater than 7 hours. There have been 1 or 2 patients that we know of who have been on the bypass for 6 hours before the insertion of the VAD and have survived, but not many.

Another variable here, however, is that we have no evidence at all in most of these cases of whether a bubble oxygenator or membrane oxygenator was used. In our early experience, and probably throughout the country, most of them were bubble oxygenators, and this would have an effect on the chance of survival according to the length of the bypass run.

There are some contraindications to the use of a VAD because of coagulation problems. If you are asked by a fellow surgeon to evaluate the patient before inserting the VAD and the patient is already having active gastrointestinal bleeding or there is evidence of intracranial bleeding, VAD insertion will probably have a disastrous result. Those patients should clearly be turned down.

A patient who has heparin antibody thrombocytopenia should also be turned down. Now, you may question this, as some VADs are said not to require heparin. Well, that's true while we are running at high flows, but to accurately wean these patients, eventually they have to be heparinized, so this is probably a contraindication.

Of course, a correlated multiple organ failure problem is that of liver failure. A patient in severe liver failure probably is going to have endless bleeding problems postoperatively.

Bleeding in association with the inability to maintain adequate systemic pressure on cardiopulmonary bypass is also a contraindication. I have been asked on a couple of occasions to evaluate such patients, and it appeared that massive bleeding was coming from all orifices. At that point it is futile to try to save that patient with a VAD. If a patient can't be maintained on cardiopulmonary bypass, he or she certainly can't be maintained on a VAD.

There are mixed figures in trying to correlate survival with the amount of blood loss in the period of time that the patient is on the VAD. In our particular series of patients, the long-term survivors actually bled more than the nonweanable patients or the short-term survivors. Again, other series show other figures: Dr Burkholder has correlated his data on a unit per hour of assist, and it appears in his cases that there is a trend that the long-term survivors have a smaller amount of overall blood loss.

In summary, if bleeding persists at the time of weaning, there is a pretty slim chance that the patient is going to survive. The bleeding has to be stopped early on, in the first 24 hours after insertion. There is no apparent significant difference in blood loss between left ventricular assist devices alone and biventricular assist devices. The addition of two more cannulation sites is not of great importance.

There is an inverse relationship, when one looks at most of the series, between heparinization and blood loss. This can be explained by the fact that, in general, most of us who see massive bleeding initially postoperatively don't heparinize. On the other hand, if we have patients with very little bleeding we are all tempted to add a little heparin just as a precautionary measure.

The final point is that the initial blood loss may not be a predictor of survival, but certainly if the bleeding isn't curtailed during the first 12 to 24 hours, disaster is usually met.

MODERATOR PENNINGTON: I am going to quickly ask the panelists a couple of questions, and then we will go to questions from the audience.

Lyle, I wasn't quite clear on one point. If you had a patient who was febrile with bacterial endocarditis, who required emergency valve replacement and wouldn't come off the pump, would that be a contraindication to placement of a VAD?

DR JOYCE: We just don't have enough cases to say one way or the other about that.

MODERATOR PENNINGTON: So if it happened to you, would you put a pump in or not?

DR JOYCE: If everything else were okay, I would; but if there were any other multiple organ failure problems or signs of anything else, I would not.

MODERATOR PENNINGTON: Fine.

Walter, we understand from you that if a 70-year-old patient in otherwise good condition has had a good operation and won't come off the pump, then you would not put an assist device in; is that right?

DR PAE: No, I think I stated previously that one must look at the general physiologic condition of the patient.

MODERATOR PENNINGTON: So you might put a pump in?

DR PAE: That's exactly right.

MODERATOR PENNINGTON: Even a 72-year-old if you thought he was physiologically okay?

DR PAE: I think that's correct.

MODERATOR PENNINGTON: Okay.

John, the first thing you said was that in your series, hepatic failure would be a real contraindication; is that right?

DR BURKHOLDER: That is correct.

MODERATOR PENNINGTON: And cerebral injury is a contraindication, of course, but if the patient didn't have it preoperatively, it is very difficult to determine in the operating room. So you wouldn't turn patients down on that basis very often, right?

DR BURKHOLDER: Absolutely.

MODERATOR PENNINGTON: Finally, what about renal failure, can you give us any concrete answers? In my criteria I had arbitrary numbers of a creatine of 3 mg/dL and a blood urea nitrogen of 50 mg/dL. How would you do that?

DR BURKHOLDER: Well, we simply have had such limited experience with preoperative renal failure in patients on heart assist that it is hard to draw any conclusions, but I think if you had a patient who was even a stable dialysis patient with no other problems and you had hope for a good outcome preoperatively and that patient crashed in the operative period, I would not exclude that patient from the possibility of postoperative support.

MODERATOR PENNINGTON: I think we would. I think we would consider dialysis a strict contraindication to insertion of the device.

Well, now let's see if our audience has some issues they would like to address.

DR BOLOOKI: Hooshang Bolooki, Miami.

I saw that Dr Joyce showed on short-term and long-term survivors some patients that had been on cardiopulmonary bypass for 130 minutes and 180 minutes. That comes to 2 hours and 3 hours. Is this support after you finished the operation or is this total support?

And the next comment I would like to hear from you is what do you think happened, because I would have continued the bypass for a few more hours before I would go to the device, if I had the device.

DR JOYCE: This is total time of cardiopulmonary bypass, which includes the period of time during which the original operation is carried out. In our early experience we prolonged bypass, many times another hour, before moving on, and practically all these patients died. We have been more and more inclined over the past year to move into ventricular assist support much earlier than we had originally, and it's only by doing so that we have had the better survival.

Now, one could argue, I'm sure, that many of these patients would have survived had they been on bypass longer, and I think that's possibly true, but comparing those two groups I think the results will be better if we become more aggressive with the use of an assist device early on.

MODERATOR PENNINGTON: Well, I think one of the advantages of VAD insertion is that once you put the device in you can stop the heparin and immediately begin to get some control of the bleeding, as well as maintain the patient on adequate flows. We have been through this many, many times, whether we should continue another hour or two of cardiopulmonary bypass. Even though we use membrane oxygenators, we are now convinced that prolonging cardiopulmonary bypass hurts more than it helps.

DR FRIST: Frist, Vanderbilt, Nashville, Tennessee.

Glenn, your data in terms of survival in perioperative infarction are enlightening and I would like you to comment on them further. Specifically, given the fact that perioperative infarctions in 24 to 48 hours have such a terrible prognostic indication, would you be more likely in those patients to go directly to the total artificial heart if you had a patient who was otherwise a good patient for transplantation or would you use an assist device?

MODERATOR PENNINGTON: I think that is an important question. Our attitude has changed somewhat about that sort of patient. When I said that perioperative infarction is a strong negative determinant, what I meant to say was that it is unlikely that the heart will recover. That does not mean, however, that we would not support that patient. Certainly if the patient was a transplant candidate, we would be inclined to use a device that would not be a replacement device but a device that would allow us to have the heart recover or, if it would not recover, maintain the patient until we could do a transplantation.

So, a perioperative infarction would not exclude a patient from support, but it would mean to us that it is unlikely that the heart is going to recover. If you didn't have the potential for transplantation in your hospital, then I think you have to consider that.

I don't want to emphasize this to the point that I would say that we should exclude all patients with perioperative infarctions from circulatory support. All I am making is a retrospective analysis of our own experience, and that's the way it's been.

DR FRAZIER: Frazier, Houston, Texas.

I would like each of the panelists to give an approximation of the percentage of patients in whom pumps were used at their institution that have the intraaortic balloon pump and are assisted by the biventricular assist devices.

MODERATOR PENNINGTON: Bud, I can answer that for our institution. We have been as high as 8% on balloon pumps with an average of about 5%, and our assist device support has been a little over 1% overall.

DR BURKHOLDER: In our institution we have in a period of 7 years used in excess of 7,000 pumps and have used the heart assist device 59 times.

DR FRAZIER: What about last year's number, do you know?

DR BURKHOLDER: In calendar year 1987, we did 1,509 pump cases and used right or left heart assist, or both, in 6 cases (0.4%).

MODERATOR PENNINGTON: So you are using it in less than 1%?

DR BURKHOLDER: Oh, yes.

DR PAE: I think our incidence of balloon pump use is about 4% and our incidence of assist device application is less than 1%. The use of ventricular assist pumping in our institution has been much higher in the bridge-to-transplantation application than it has been for postcardiotomy cardiogenic shock.

DR JOYCE: Our use of the intraaortic balloon has been in the range of 5% to 10% and the VAD support has been less than 1%. We have used it six times in the last 1,000 cases.

DR FRAZIER: Well, that's interesting. To me, the hardest thing in this field is to decide who to use it on. At the Texas Heart Institute last year we used 3,300 pumps and we had 200 intraaortic balloons (about 1.5%); 0.2% of our patients received more advanced assist. I don't know if those numbers should be higher or lower, but I think they point out the disparities in the numbers, which are considerable, from the different centers. I think this indicates the problem we have in deciding exactly when to intervene and in whom to use these devices.

MODERATOR PENNINGTON: One of the important considerations is the tendency to try to get the patient out of the operating room by whatever means possible. We are all aware that in many cases a borderline patient can receive the polypharmacy treatment and intermittent epinephrine injections, get out of the operating room, and actually make it to the intensive care unit, only to die of multiple organ failure over several weeks. So, I think one has to carefully analyze all the information in deciding whether these pumps are indicated or not.

I know that we haven't answered all the questions of patient selection, but as we go through the morning, I am sure many of these issues will come up again.

Thank you very much, panelists, for that discussion.

Panel 2
Intraoperative Management

Moderator: J. Donald Hill, MD
Panelists: Robert L. Hardesty, MD, William A. Baumgartner, MD, and
Daniel M. Rose, MD

MODERATOR HILL: Good morning. I am Don Hill from Pacific Presbyterian Medical Center in San Francisco, and I would like to introduce our panelists here. The panelists are Bob Hardesty from the University of Pittsburgh, Bill Baumgartner from Johns Hopkins University, and Dan Rose from the Health Science Center in New York.

As you are going to hear repetitively over the next two days, success in this technology really depends on three things: the selection of patients, the performance and selection of the device, and the skill, experience, and judgment of the surgeon who is using these devices.

What we are going to concentrate on in this panel is the intraoperative use of these devices, how you select them, how you use them, and, hopefully, a lot of the tricks and experiences that have been successfully learned, sometimes through some very hard events.

One of the things that you have to keep in mind with these devices is that they sustain life and they do not create life. You have the idea sometimes that they are going to resurrect the dead. They are not going to do that.

Second, you should always keep in mind that the device itself has to fit the patient. You can't expect the patient to fit the device. That has been a hard lesson for us to learn, and I think anybody who has had experience in this sometimes expects too much of the patient. You have to make your expectations and choices of the devices.

Now before we begin, I would like the panelists each to identify the devices or the systems that they have had experience with, so you will know where they are coming from, and the approximate numbers. Dan?

DR ROSE: This is combining two institutions, New York University and Maimonides Medical Center in Brooklyn. We have used primarily the roller pump assist device and we're close to about 90 patients, both right and left ventricular assist. We haven't used that except on one occasion as a biventricular assist. We are now just using a centrifugal pump, because it's a little bit easier to use and we finally had the money to purchase one (although it's not that expensive).

MODERATOR HILL: Bill?

DR BAUMGARTNER: Well, we have experience primarily with the centrifugal pump and have used it in 13 patients; we have limited experience with the Novacor left ventricular assist system.

MODERATOR HILL: Bob?

DR HARDESTY: Our primary experience has been with total replacement using that as a bridge to transplantation. We have a very limited experience, 3 patients, I believe, where we have used the centrifugal pump after a failed transplant, and a very limited experience in extracorporeal membrane oxygenation (ECMO) as well. We did have one experience with the use of the Novacor device as a bridge to transplantation as well.

MODERATOR HILL: At Pacific Presbyterian Medical Center we have had experience using the Thoratec/Pierce–Donachy pump in about 20 patients and centrifugal pumps in about 30, and we have had about 40 ECMO patients. Many of the ECMO procedures were for respiratory support; some of them were for cardiac support.

Now, what we're going to do is to take a scenario in an operating room and try to work through how we would actually manage it and try to touch on some of the real surgical details that become important in success.

So, Dan, you're in the operating room, it's three o'clock in the afternoon, you have a patient that you thought was going to be straightforward, and it turns out that you have a problem. The patient is 64 years old and weighs 70 kg. He came to the operating room with 4+ mitral regurgitation, and he had an ejection fraction of 33%. He had no coronary artery disease. You did a good operation, you were satisfied, but the ventricle just couldn't do it when you took the patient off bypass, and you have used a sequence of drugs. What are you going to do?

DR ROSE: Obviously, I didn't do the operation that well. (Laughter.)

Obviously, you have to go through the sequence of events. Are there any technical problems? Did you injure the coronary artery? Is there some problem with the valve; if you used a mechanical valve, is it opening properly?

So, obviously, you don't want to discuss those things. You have to decide, if it's purely a failure problem, is it left ventricular failure or is it right ventricular failure, or is it both? Sometimes it's difficult to distinguish these things.

Obviously, you already probably put in a balloon pump and tried the various combinations of pharmacologic agents, and the patient still couldn't come off bypass. We don't always put in a left atrial line, but certainly in this person I would put in a left atrial monitoring line, and that

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would help you sort out additionally if it was purely a right-sided problem or initially a left-sided problem. If you took the patient off bypass and he or she had high left atrial pressures or you couldn't bring the patient off bypass, but in attempting to end bypass you saw high left-sided pressures, you would be concerned that initially you would be dealing with a left-sided problem.

Anyway, if you are pretty certain that you are dealing primarily with a left heart failure or biventricular failure, what we would do is insert a left heart assist device. In this case it is a little bit tricky where you are going to put your left atrial cannula, because you have your mitral suture line. In some cases we will go through the left atrial appendage. Again, if you have the mitral valve in place, you may not want to elevate the heart due to potential problems with atrioventricular disruption. I probably wouldn't put the cannula right through the suture line, but maybe go out a little bit into the right superior pulmonary vein and put in a pursestring suture with pledgets. We would generally try to put in a 28F or 32F venous cannula through that pursestring suture.

MODERATOR HILL: Is that right-angled or straight?

DR ROSE: We have used both. You can use either one. If you have a right-angled one, you don't want it too long because it could injure the valve. You would maybe have that about 3 cm in length. But a straight one also you don't want to push in too far because it can obviously go out into the pulmonary vein or something of that nature.

MODERATOR HILL: Would you ever go to the atrial appendage?

DR ROSE: In coronary patients we have done it on a number of occasions. In a patient with a mitral prosthesis I would be a little bit reluctant. Maybe you have done it and had no problems. If you have ever had an atrioventricular tear, you don't ever want to see another one. So I would be a little bit reluctant to put the cannula in the left atrial appendage in a patient with a mitral valve prosthesis.

MODERATOR HILL: Do you use a double pursestring suture?

DR ROSE: Yes.

MODERATOR HILL: With a tourniquet?

DR ROSE: With a tourniquet; leave the tourniquet in, and then when you come back you can just tie it off.

MODERATOR HILL: What about your arterial return?

DR ROSE: Well, we put in a separate arterial cannula and it's a smaller cannula. We used to use a pediatric endotracheal tube, and we have gone to a small, tapered BARD cannula. We have always thought—although we have never had any evidence for this—that it was important to slip the cannula a little bit down into the arch in case there was some problem with thromboembolism, then at least you wouldn't shower stuff to the brain.

MODERATOR HILL: Where would you bring the cannula out?

DR ROSE: Well, we used to make a big deal out of bringing it out of a separate stab incision so that we could try to close the sternum. You can bring it out through the sternum if the sternum comes together nicely and it doesn't compress the heart. This is something you have to be very careful about because you want to avoid any sort of either pericardial or sternal or soft tissue or skin compression on the ventricle. You can just bring it right out through the incision. Sometimes you can remove a little bit of the sternum with a rongeur and put in a couple of wires and it will close and won't alter the hemodynamics. Sometimes you have to leave the whole thing wide open.

MODERATOR HILL: Bill, what would you have done? Anything different here?

DR BAUMGARTNER: Well, we would use the same approach for the venous cannula and use a 32F reinforced cannula in the right superior pulmonary vein. We would put in, again, a 22F BARD cannula in the aorta. On all our cases we have been bringing the cannulas out through a separate stab incision, because, considering that these patients might go on to transplantation, we are very concerned about infection. Of the survivors that we have had, and not only the ones who have survived and been discharged from the hospital but the ones who have been weaned from the device, we have had no mediastinitis using this technique. So we have closed the chest on each individual patient.

MODERATOR HILL: I didn't understand whether you bring the cannula straight through the incision or out through the intercostals or the inferior part of the wound.

DR BAUMGARTNER: Very much like the chest tubes, through the inferior part of the wound.

MODERATOR HILL: Bob?

DR HARDESTY: I really don't have much to add. I think, again, the circumstances under which we are asked to see patients, particularly locally, is as a consideration for transplantation after they have been placed on ventricular assist. Currently our position is that we would not do that if the sternum is not closed and we would not accept a patient if in fact the cannulas are coming out over the superstemal notch. So, again, I think it is very important that the cannulas exit much like the chest tubes and that the sternum be closed.

MODERATOR HILL: Does everybody agree that it is good to close the sternum, if possible?

DR ROSE: I think it is a good idea if you can, but occasionally you are going to have patients in whom you can't, and there are various things you can do in that situation. Some people have recommended just taking a piece of Silastic and sewing that around the sternum. What we have done sometimes is just pack it with sterile gauze and usually in about 48 to 72 hours you can close the sternum. But sometimes it's very impressive: you can't even close the skin without markedly compromising the hemodynamics.

Let me ask you a question. With the Pierce–Donachy, that right-angle cannula, do you put that through the atrial appendage in patients with mitral valves, or have you?

MODERATOR HILL: We have and we would.

I was going to throw that question back. If this patient had not had a mitral valve, would you make any distinction in whether you went to the atrial appendage or through the superior pulmonary vein?

DR ROSE: I think for me, it is more what is technically easier. If you have a large hypertrophic ventricle and very small appendage, sometimes it's very difficult to get to the appendage. Other times you will have a nice small ventricle and big appendage that is sticking up there and is very appealing to the surgeon.

MODERATOR HILL: Does everybody go back to bypass under these circumstances to put their cannulas in or do you try to do these cannulations without bypass?

DR ROSE: We will almost always put the patient back on bypass.

MODERATOR HILL: What about removing air from the pump, how would you remove the air from your bypass system?

DR ROSE: Well, we have a little reservoir sort of as a trap, and you can remove air that way. Then the perfusionist just runs a closed circuit and gets the air out. When you divide the cannula and you connect your cannula to the tubing, you inject saline and . . .

MODERATOR HILL: Push it together?

DR ROSE: Right.

MODERATOR HILL: Does everybody do it that way? Bill?

DR BAUMGARTNER: Yes. Well, to answer your questions, I think the place to put the venous cannula is—I agree with Dan—whichever is the easiest, because you're going to come back and have to take it out. You have to think ahead, because if the patient has a big left ventricle it's going to be much easier to put the cannula in through the right superior pulmonary vein, and clearly it is easier to leave a pursestring suture in the area so that you don't have to fight to put that in when you come back in again. We always put the patient back on bypass. It makes putting the cannula in very quick. The whole procedure from the time you start to the time you have the patient on a left heart assist should be somewhere in the range of 20 to 30 minutes so that by the time you have these cannulas in place the perfusionists have arranged to have the pump. The maneuver for removing air from the centrifugal pump is actually quite easy. The pump has a recirculation system and you just knock out the bubbles during the recirculation and bring it right on. We have not really had any problems during that.

MODERATOR HILL: Do you take any precautions when you first go from one support system to the other to avoid sucking air into the cannula sites? Do you put them under blood or fluid, or do you just start up?

DR BAUMGARTNER: Well, actually, most of them, as you know, are under blood whether you want it or not (laughter), and so I think that is a self-answering question. We actually take it slow and come down on cardiopulmonary bypass while coming up on left ventricular flow. If you do that in a nice controlled situation, the patient should come off bypass fine. Of course, we look at the right-sided hemodynamics at that point.

DR ROSE: I think that is a very important point that you just sort of gloss over. Usually it's not a problem, but if you go on left heart bypass too quickly and the left atrium is collapsed or empty, you can create a vacuum and embolize massive amounts of air.

MODERATOR HILL: In which case, the case is over.

DR ROSE: Right.

MODERATOR HILL: Bob, do you have any comments on this?

DR HARDESTY: I think everything has been said.

MODERATOR HILL: Say you had this patient who had a mitral valve and you put three grafts in him, on the right pulmonary artery, the LAD, and the circumflex. If the cannulas cause space to be a problem, do you do any special thing to protect those grafts from the cannulas and chest tubes? How do you optimize the space in there so you don't get compression either of the heart or of the grafts? Dan?

DR ROSE: First you have to find a place to insert your arterial cannula, and if you go out on the arch a little ways, there is usually room there.

MODERATOR HILL: How far peripherally will you go into the chest; would you bring the cannulas through intercostal spaces to protect your grafts?

DR ROSE: I have gone out, not quite out to the midclavicular line, but I have gone out there. You open the pericardium wide and the pleural space is wide. Usually I haven't had that much of a problem in terms of a compressing graft.

MODERATOR HILL: Bill?

DR BAUMGARTNER: Well, I agree with Dan. We have not had a problem with that. Our grafts that come off the aorta come off on the left lateral and right lateral surface and none of them come off anteriorly, so when we put the aortic cannula in place, it usually does not come into contact with the proximal anastomosis. And if you use the right superior pulmonary vein, the only vein graft that you have to be concerned about is the graft to the right coronary artery, and that, at least so far, has not been a problem.

MODERATOR HILL: Bob?

DR HARDESTY: I have no experience.

MODERATOR HILL: I think I would just comment on what our experience is and what we consider a priority. We consider it a priority to close the chest because it has a lot to do with bleeding, with infection, and with nursing care. It is obviously a priority to keep any graft open. In knowing that, we will do a lot to create space in the anterior mediastinum so that we can close the chest without having a graft compression. Therefore, we will bring chest tubes out almost always from the periphery going through the chest and come across so that we don't jeopardize the wound. We will bring up cannulation sites peripherally as well. If we have a lot of space, we will bring them out inferiorly and use right-angle cannulas.

Suppose now we have another situation, and that situation is one that we are seeing more and more because of the activities that are going on in the catheterization laboratory. It's three o'clock in the afternoon and they call you about a patient in the catheterization laboratory who is 44 years old and has an aortic stenosis. Somebody said, "We'd like to know what the coronary arteries look like," and they dissected the main left coronary artery. They call you, they have a cardiac arrest, they're massaging the patient, he's 44 years old, and you walk down there. What are you going to do? Bob?

DR HARDESTY: I think I'd like to defer on that. (Laughter.)

MODERATOR HILL: I think that is a common answer. Bill?

DR BAUMGARTNER: Obviously, that's a tough situation. You've got a young man, you've got someone who is presumably in full arrest. It's unlikely that that patient is going to survive. However, I think that in a situation like that, if we had that and whether or not we had an operating room available, we would go ahead and put in a device—we have the CPS system—and then transfer that patient up to the operating room.

MODERATOR HILL: CPS, what is it?

DR BAUMGARTNER: Well, it's basically a portable ECMO system. I mean, it's available, and I think Glenn Pennington has made one up. One is made available through BARD, and we would use that and bring that patient up to the operating room.

I must say that in the whole time that I have been doing this, we have not had a case at all similar to that scenario. But an older patient like that, a patient in his 60s or 70s, I wouldn't do it.

MODERATOR HILL: Dan?

DR ROSE: I agree with Bill. I think the best thing to do in that situation is to get the patient on bypass as quickly as you can, preferably in the catheterization laboratory with the portable setup, particularly if you have critical aortic stenosis, you know, closed chest massage, along with coronary dissection.

I think Bill raises a real interesting point. In the current age of all the scrutiny going on, if you had a patient that was a little bit older, in the 60s or early 70s, what would you do? Would you go all out or would you just not do anything?

MODERATOR HILL: Well, for the purposes of this discussion, we should say that we are going to do what we can do, so what would you do?

DR ROSE: In the older patient, a patient in his 70s, it's a tough question. I am going to defer.

MODERATOR HILL: Let me ask you another one. Do you have a system that is set up near a catheterization laboratory or through your perfusionists so that in short order you can get the patient on bypass from any part of the hospital—postoperative heart surgery patients, critical care unit patients, catheterization laboratory patients—do you have a setup like that?

DR ROSE: We have a setup down in the catheterization laboratory. We don't have one in our open heart unit. We have a portable system and we have used it, I think on two occasions, on patients who we thought had massive pulmonary emboli that arrested on the floor. We didn't salvage either of them.

But I think, particularly with this new BARD system, that you are going to see more and more systems like that, portable bypass systems, because it's really not much more difficult than inserting an intraaortic balloon, and it's probably the best way to resuscitate some of these patients.

MODERATOR HILL: Bob, do you have a system in Pittsburgh?

DR HARDESTY: We do not have a portable system nor are we prepared to immediately support somebody who has a failed angioplasty.

MODERATOR HILL: Bill?

DR BAUMGARTNER: We have a system that sits up in the operating room and we feel it ought to stay up there as opposed to sitting right next to the angioplasty suite so that we have control over it. (Laughter.)

Not to drag this into the ground, but, honestly, the data available that John Burkholder and other groups showed demonstrate that with patients who are older than 70 years, if you take those patients and compress them on the chest to the operating room, their chances of survival are bleak. So if an older patient has them, in that situation I will go on record that we would not go ahead and pursue that.

MODERATOR HILL: Let's take another scenario of a 44-year-old lady who has an ejection fraction of 9%, weighs 70 kg, has two Wood units, and is sitting in the hospital waiting for a transplant. She has had runs of ventricular tachycardia and ends on dopamine, and everybody is getting very nervous.

Bob, what do we do in Pittsburgh?

DR HARDESTY: Well, up to the present time we have waited until the very last moment before we elected to place this patient on assist, and up to this point, of course, our approach has been total replacement. However, I think the results currently indicate to us that this patient is a very good candidate. The ventricular arrhythmia is of some concern and probably today, based on our most recent experience, we would act sooner rather than later. In the past we would have waited until she was being resuscitated and then take her to the operating room to replace her heart with the artificial device as a bridge. I think currently, and particularly with the ventricular arrhythmia, in this circumstance as soon as we see any deterioration of her renal function or if the ventricular arrhythmia is not manageable, I would replace the heart and then bridge her.

MODERATOR HILL: Replace?

DR HARDESTY: Use the total artificial heart.

MODERATOR HILL: Bill?

DR BAUMGARTNER: Well, I couldn't agree with Bob any more.

I think in the case of a patient who is a transplant recipient and has congestive heart failure and progressive deterioration, that is a much easier scenario to know when to intervene.

Regarding the patient with arrhythmias and malignant ventricular tachycardia, I think if you go through the motions of the drugs and that is not working, then that patient ought to have a device put in. And with that kind of patient, an elected patient, we would go ahead and put in a Novacor system.

MODERATOR HILL: What if the patient had a significant right ventricular failure associated with it?

DR BAUMGARTNER: Well, at that point I think we would still go ahead and put in the Novacor, because that is the device that we have, and evaluate it at the time of placement. And if indeed the patient clearly had right ventricular problems despite the unloading that the Novacor device provides, then that patient would have to be placed on a right-sided centrifugal device.

MODERATOR HILL: And you would sort of press yourself into that; you would try it first and if you couldn't manage it, then you would go to a right-sided device?

DR BAUMGARTNER: Right.

MODERATOR HILL: At Pacific Presbyterian Medical Center we would not do it differently than that. I think everybody agreed that once you get into that scenario, you have to do something or you are going to have a patient that is just going to die on you at some moment; you want to support the patient until you get a device. We have used two Thoratec pumps. I don't think that we would only put a pump in on the left side; we would also put one in on the right because we don't find that it increases morbidity, and it certainly makes the management a lot easier in the postoperative period in terms of the nurse seeing the drugs. Everything surrounding the patient becomes easier under the scenario.

Although they are going to touch on this in the next session, I don't think enough can be said to draw from surgeons' experience about the issue of bleeding after you put in any kind of device. It doesn't really matter whether it is a total heart, a heterotopic heart, or centrifugal pumps. When the patient comes off bypass, you have problems with bleeding, and it is pretty crucial to eliminate that in the postoperative period.

So, how do you manage this in Pittsburgh, Bob, in terms of bleeding? I will exclude one thing at the beginning: we are assuming that it is a good operation and that you don't have obvious bleeding leaks from anastomotic lines that you are obviously going to repair. What kind of drugs or tests do you use, what kind of tricks do you do to control hemorrhage?

DR HARDESTY: First, we obviously would reverse the heparin. If we are still having significant bleeding problems, the primary mainstay is the activated clotting time. If that is normal and we still feel that we have a coagulopathy, the thromboelastogram has been very helpful.

There is a large experience with the liver transplantation program and the use of it, and we get assistance from the anesthesiologists, who are very good in interpreting it. They can give us an idea as to what the coagulation defects may be and replace the coagulation factors according to the thromboelastogram and what it indicates.

On the other hand, it usually boils down to the fact that we end up giving fresh frozen plasma, cryoprecipitate, and platelets in spite of that. After the transfer to the intensive care unit—I don't know whether the question relates to the management of the anticoagulation.

MODERATOR HILL: Let me ask you one thing. How long would you hang in there, and how important do you believe it is to sort of have everything controlled before you leave the operating room? Are you willing to continue to manage the bleeding problem in the recovery room?

DR HARDESTY: That's tough. I think for the most part we would wait it out in the operating room because anytime that we haven't, we have regretted it. We take them back to the intensive care unit, then end up coming back again under uncontrolled circumstances. So I think we do our very best in the operating room, and that's where we have our best support in terms of the replacement of the coagulation factors.

MODERATOR HILL: Bill?

DR BAUMGARTNER: Well, we could do the same thing. I think it is important when you take that patient back to the intensive care unit that bleeding is under control, and I think that was pointed out in the earlier presentations about its bearing upon survival.

When the patient comes off bypass and onto assist, we will give a protamine partial dose to reverse the activated coagulation time and bring it down to around 200 seconds. We will do that initially to see if that by itself will help us out. We will use the usual armamentarium of fresh frozen plasma and platelets.

We have had reasonable success using a fibrin glue as part of the program. The other drug that we have not used with left ventricular assist, although I have spoken to our hematologists about it, is desmopressin. We have used desmopressin for routine cases and reoperations, and maybe it is just us or maybe it is just subjective, but we think it works. I talked with our hematologists, and they do not think there would be any influence upon the activated coagulation time. So I think that is another potential trick that you can use in these patients. The important thing, I think, is to stop the bleeding as much as you can before taking them to the intensive care unit.

MODERATOR HILL: Dan?

DR ROSE: I don't have many data. I think I would just like to underscore.

One of the ways you get into the problem is by just putting the patient on and off bypass and prolonging bypass unnecessarily. I think one of the ways to minimize your bleeding problems is to avoid prolonging cardiopulmonary bypass.

Second, I think it is important to repeat what the other discussants have said. I think it is much better to stop the bleeding as much as you possibly can in the operating room than try to tough it out in the intensive care unit, because otherwise tamponade will usually develop and you will be opening up the chest in less than ideal conditions.

MODERATOR HILL: I can't add a lot to that. I think it is mandatory to control bleeding in the operating room. You are just kidding yourself if you think it is going to be a better scenario postoperatively. It is just much more difficult to manage. The only thing that we would use is powdered Gelfoam, which we use on the wound to help stop oozing; we would not uncommonly use positive end-expiratory pressure as well, just so that everything is a little bit more compressed, if it isn't already compressed.

I think I will open the panel up for questions. We will take one question. Does anybody have a burning question?

DR KRONCHAY: Kronchay from Albany.

The question I have is, if you have a patient who needs a left heart assist device, what is the incidence of right heart failure associated thereafter?

Do you see a lot of that; and if you do, do you sort of prophylactically put in a right assist device at the time or do you have to bring them back and forth?

MODERATOR HILL: Well, I will answer that question myself.

Our attitude is that if you suspect right heart failure—and you usually do it on a trial and error basis; sometimes you will obviously know but if you don't really know, you do it on a trial and error basis—then you should always put a pump in because putting it in doesn't add a lot. It's sort of a nuisance and you wish you didn't have to do it, but do it because it will make the world much better for you an hour or two later in the recovery room when you are not struggling with a right ventricle that doesn't work.

Bob, do you want to comment on that?

DR HARDESTY: I agree.

MODERATOR HILL: Bill?

DR BAUMGARTNER: Well, I would agree that that is our scenario. We would definitely assess it, though, according to the sort of statistics and criteria that Glenn showed. That is, put the left ventricular assist device in and then see if you can maintain flows adequate to give you a cardiac index of greater than 2 $L/min/m^2$ and a right atrial pressure of less than 15 mm Hg or a little bit more. You also look at the right heart. I think that it is real important to look and see what the right heart is doing, and you can then make that assessment at the time.

MODERATOR HILL: Dan?

DR ROSE: I agree. We probably have underused the right heart assist device in a number of patients. We should have used it.

MODERATOR HILL: Thank you very much, panelists, and I thank the audience.

Panel 3

Bleeding and Anticoagulation

Moderator: Jack G. Copeland III, MD
Panelists: Laurence A. Harker, MD, J. Heinrich Joist, MD, and William C. DeVries, MD

MODERATOR COPELAND: I think we all as surgeons and allied personnel have a love-hate relationship with the coagulation system. It seems to me I spend most of my time trying to stop bleeding.

We have this morning a learned panel to discuss bleeding and anticoagulation. First I would like to introduce them.

On your right is Dr William DeVries, who, of course, needs no introduction, a pioneer in the total artificial heart.

Next to him is Laurence Harker, who is chief of the Division of Thrombosis and Arteriosclerosis at the Scripps Clinic and has been an advisor to us on the national cooperative study of aspirin and coronary artery bypass grafting. He is certainly a platelet specialist.

And next to him is Heinrich Joist, who is professor of Medicine and Pathology and chief of Hematology at the St. Louis University Medical Center. He has been there since 1978 and has extensive experience working with Dr Pennington's program.

What I would like to do with this session is divide it into three short segments of 15 minutes apiece and focus for ten minutes on the panel discussion and five minutes on discussion from the audience.

The three areas of general discussion that I think are appropriate are routine cardiopulmonary bypass and its effect on the coagulation system, ventricular assist devices and their management, and the total artificial heart.

What I would like to do is to start off by peppering each of our panelists with some questions. We'll have Dr Harker lead off as he is an expert in the area of the effects of cardiopulmonary bypass on the clotting system.

First of all, Laury, let me ask you, what effect does the length of the pump run have on the coagulation system, and does it make any difference whether you use a bubble oxygenator or a membrane oxygenator?

DR HARKER: Well, the length of the bypass certainly has a major effect on the hemostatic function of the platelets.

As you know, during bypass heparinization will certainly prevent the conversion of fibrinogen to fibrin, but it does not affect platelet function, as you can demonstrate by having a normal bleeding time after the heparinization process. However, thereafter there is a progressive prolongation in the bleeding time that becomes greater than 30 minutes by 2 hours of bypass. That means that it extends beyond the sensitivity of that test to assess the hemostatic function of platelets. It has been shown that this is a consequence of the activation process of the platelets interacting with the oxygenator, and that the platelets then become refractory and dysfunctional. The responsiveness to AGNES in the aggregometer is clearly abnormal. Fortunately, there is normalization of the hemostatic function of the platelets over the course following discontinuance of bypass within 30 minutes or so. Thus, the duration of bypass is very important with respect to hemostatic function of platelets. The shorter you can make it, the better.

Regarding the question about bubble or membrane oxygenators, experimentally they are equivalent, in our hands, with respect to their effects on platelet dysfunction.

MODERATOR COPELAND: So you would say that the major effect of cardiopulmonary bypass on the hemostatic system is on the platelets. What about the clotting factors?

DR HARKER: Well, the only thing that happens to the clotting factors, as far as we can tell, in a heparinized individual is that they become diluted to half once you go on to the nonblood prime in the oxygenator. Now, that doesn't reduce those factors below hemostatically competent levels. Therefore, that dilution has no known effect on hemostasis in the usual patient.

MODERATOR COPELAND: So let's take a scenario in which a patient has gone to the operating room and things have not gone well; the pump run has gone over two hours and we're beginning to think about ventricular assist devices and that type of thing. We're seeing a problem coming up in the very near future of massive hemorrhage.

How would you go about dealing with a patient in that situation? Let's say he had been on bypass for three hours and he has a ventricular assist system in place. Now, what do we do? He's bleeding to death.

DR HARKER: The major problem in patients that have been appropriately neutralized with heparin is clearly platelet-related inadequate blood clotting. There is a combination of thrombocytopenia and dysfunction.

In normal circumstances, when platelets function normally, a count of 100,000/μL will give a normal bleeding time and adequate hemostasis of the platelet-dependent variety. If the count is below that, then certainly you are going to need transfused platelets.

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Indeed, there may be platelet dysfunction as manifested by very long bleeding times and then platelets may have to be given even though the count is greater than 100,000/μL.

We have found that desmopressin is also a very useful adjunct in improving platelet hemostatic plug formation, but you have to remember that you get one shot. You will get a duration of effect of 30 to 60, sometimes as long as 90 minutes, so you better make sure that the timing is appropriate.

Subsequent administration of desmopressin will not give a comparable improvement in the bleeding time until the next 12 to 24 hours.

MODERATOR COPELAND: I'd like to hear comments from the panel on this scenario, the patient after prolonged bypass time who is massively bleeding. Bill?

DR DEVRIES: We do about the same things, being sure that whenever we have one of these patients we preoperatively make sure that there are plenty of platelets available for use during that period of time. We use desmopressin too on the artificial heart, and it has worked very, very well.

By the time we end bypass fibrin glue seems to be a good thing to use. Occasionally it's hard to get into the back of the recesses of the heart, but any type of mechanical method is important.

I think the main thing to do is to work out a protocol before you go in there on these cases. The surgeon at that point is in a real swamp of alligators and it is time to have a real coordinated effort between the anesthesiologists, those responsible for blood replacement, and all the people who perform the tests that they need. You need to be sure that they know what desmopressin is and that they have read the package inserts, that they know when to give the platelets, and that everything is in order.

I would emphasize that establishment of the protocol and doing most of the work before you get into this problem is probably the most critical. Making sure the hematologist gets up and gets there and knows what to do is really very important during these times.

MODERATOR COPELAND: In your protocol do you give a certain number of platelets? Do you replace with fresh frozen plasma? Do you use anything else like Konyne?

DR DEVRIES: We use a 20-pack of platelets and plenty of fresh frozen plasma. After we first neutralize with protamine and the patient continues to bleed, then we go to the next step, which is the platelets and the fresh frozen plasma. After that fibrin glue and those sort of things can be used at the operative site.

MODERATOR COPELAND: Dr Joist, what would your recommendations at the University of St. Louis be in this situation?

DR JOIST: We generally handle the situation in a fashion very similar to that described by Dr Harker and Dr DeVries.

I might make two additional comments. One is that hematologists are generally of limited help in the acute situation in the operating room, because by the time they arrive or otherwise get involved, they will ask for laboratory values that may not be available. My belief is that acute, excessive bleeding needs to be managed by the team in the operating room. Initial decisions on measures to control bleeding must take into account the patient's preoperative clinical condition and laboratory evaluation (platelet count, bleeding time, activated partial thromboplastin time [aPTT], prothrombin time [PT], fibrinogen) as well as time on bypass.

The second point I would like to make is that some blood banks have a standing order that they will not release platelets unless you can document that the platelet count is below a certain number, such as 100,000/μL. It is important to make arrangements with the blood bank that bypass cases are exempt from this particular rule. These cases should also be exempt from the policy that no more than six units of platelets may be released at a time. As Dr DeVries has pointed out, not infrequently one may need more than six units to raise the platelet count to greater than 100,000/μL, a goal that we follow in general.

In a critical situation like this, my philosophy has changed over the years from being very conservative in giving blood products, particularly platelet concentrates, to making maximum efforts at rapid control of bleeding. Even if one gives a bit too much at times, it is better than to go with a piecemeal approach and possibly have a patient continue to bleed for hours and hours. I would like to see the platelet count clearly above 100,000/μL and a normal aPTT and PT greater than 50% activity or less than 1.2 times the normal control PT in a patient with continued excessive bleeding before making the decision to reexplore.

The third point I would like to make is that decamino-D arginine vasopressin (desmopressin, DDAVP) appears to be a useful agent in certain cardiopulmonary bypass patients [1, 2]. Salzman and associates [1] carried out a randomized, double-blind study in which DDAVP or placebo was given prophylactically preoperatively to adult patients undergoing complicated coronary artery bypass operations (valve replacement and coronary artery bypass graft, repeat coronary artery bypass graft), valve replacement, and operation for atrial septal defect and observed a significant reduction in intraoperative and postoperative blood loss with DDAVP. In the study by Czer and colleagues [2], which was not randomized or placebo-controlled, DDAVP was given to adult cardiopulmonary bypass patients (including patients receiving primary coronary artery bypass grafts) with excessive postoperative bleeding and a prolonged bleeding time who had a negative past history for abnormal bleeding, a normal preoperative hemostatic evaluation, and had not taken aspirin within seven days of operation. Decamino-D arginine vasopressin appeared to be as effective in controlling excessive bleeding as transfusion of platelets and fresh frozen plasma, as reflected by a 50% reduction in the use of these blood products in patients treated with DDAVP. I believe that the data from this latter study should be confirmed by data from a randomized, controlled study that should include patients with current or recent use of aspirin before DDAVP can be generally recommended. It should also be noted that, in contrast to these rather impressive results in adult patients, DDAVP does not seem to be effective in reducing blood loss in children undergoing cardiopulmonary bypass operations [3]. As far as the use of DDAVP in patients with ventricular assist devices (VADs) is concerned, there seems to be no published information. At the present time it seems reasonable to use DDAVP in patients with VADs to prevent or control excessive bleeding, but the effectiveness of this approach remains to be established.

Finally, DDAVP essentially has an effect on only one particular set of hemostatic factors, and this is the Factor VIII complex, consisting of Factor VIII:C (coagulant activity) and von Willebrand factor. As Dr Harker just pointed out, the increase in these two factors induced by DDAVP is rather transient. If the overall coagulation system is such that major dilution or consumption, or both, has taken place, associated with depletion of factors other than factor VIII and vWF (such as factor V and antithrombin III), as we have seen particularly in some patients with VADs, DDAVP is not likely to be effective in controlling the abnormal bleeding. In such a case fresh frozen plasma should be administered, which of course contains all of the clotting factors and inhibitors.

MODERATOR COPELAND: Can I ask just one thing of you, Laury, before you comment further? How soon can we expect these platelets that we're giving to have an effect on hemostasis? We're assuming, of course, that the operation has been okay and that all the mechanical factors are controlled surgically. How soon are the platelets really going to come to the rescue?

DR HARKER: Most blood banks at the present time use room temperature–stored platelets, and they are maintained in plasma with constant mixing at room temperature. When those platelets are infused, they will not be fully functional at the time of infusion and may require 15 to 30 minutes before they have full hemostatic competence. If you can obtain platelets that have been harvested within hours, they will perform immediately upon transfusion. So there is something of a burden, but I don't think that it is possible in most circumstances to get fresh platelets.

I would like to make one other comment, a real plea for replacement with whole blood or at least an appropriate combination of plasma and red cells to maintain your volume requirement. If you do that, then you will virtually never have to make transfusions with cryoprecipitate or worry about Factor V replacement. You will just have all of the clotting factors that you need. They're appropriate if you maintain volume replacement with whole blood or the equivalent.

And the last point I would like to make about the desmopressin story is that the data that justified this, of course, are related to the control trial that Salzman and his colleagues carried out that was reported in the *New England Journal of Medicine*. In this randomized trial there was reduced bleeding in association with regular desmopressin administration. But nobody really uses it in that way. The way in which it is used is reflected by the study that came out of Cedars Sinai, in which they looked at the bleeding time and bleeding in individuals who had bleeding problems and did or did not get desmopressin. They were able to show that you could shorten significantly the bleeding time when desmopressin was given in such patients and that their bleeding would be reduced.

I think that the data available, together with the demonstration that desmopressin administration causes a nonspecific improvement in bleeding time in patients that have a wide variety of platelet dysfunctional problems, support the notion that this is likely to be a very useful adjunct as long as you keep in mind that you get one shot and that it doesn't eliminate thrombocytopenia or other kinds of problems.

DR DEVRIES: Let me just say one thing. Platelets are great, but one of the problems you have to watch with your anesthesiologists is the fact that sometimes they can be intensively vasoactive. Twenty units of platelets or ten units of platelets may drop the patient's systemic vascular resistance from 2,200 to 200. And if you are giving platelets and all of a sudden unexpectedly you find that the patient's blood pressure is 40 mm Hg, be very, very wary that that is probably due to the vasoactive preparation of the platelets. Be prepared at that time to administer epinephrine or whatever you have to, because administration of a bolus of platelets like that into the body in this period of time, when the pressure is bouncing up and down, can sometimes cause problems. You have caused hemostasis, but it may be because the patient's pressure is 20 mm Hg.

MODERATOR COPELAND: Any comments or questions from the audience on the general area of bleeding and anticoagulation after cardiopulmonary bypass?

DR JUDSON: John Judson from Harrisburg, Pennsylvania.

Has anyone noticed any differences between the manufacturers of protamine? We think we see some differences between the protamine made by Lilly versus LyphoMed versus Quad. Has anyone else noted that?

MODERATOR COPELAND: No.

DR DEMBITSKY: Dembitsky from San Diego.

Could the hematologists comment on the efficacy of Amicar in this situation?

DR JOIST: I know of only one controlled, prospective study that has been done with respect to the effectiveness of ϵ-aminocaproic acid in controlling excessive bleeding with cardiopulmonary bypass, and that is the study by McClure and Izsak [4] in children with congenital heart disease. ϵ-Aminocaproic acid administration was associated with an almost 50% reduction in total postbypass blood loss in children with cyanotic heart disease, whereas total blood loss in noncyanotic children was similar in the ϵ-aminocaproic acid and control groups.

The rationale for routine use of Amicar in bypass patients would not seem to be strong, because in several studies in which fibrinolysis in patients on bypass and after bypass was carefully examined [5, 6] increased fibrinolysis was a very rare finding and thus probably plays no significant role in the acute bleeding problems in these patients.

Furthermore, Amicar is not an innocuous agent, and blocking of the fibrinolytic system with the systemic administration of Amicar might predispose the patient to thromboembolic complications.

MODERATOR COPELAND: What about in chronic cyanotic patients? Isn't there increased fibrinolytic activity sometimes in them?

DR JOIST: Hemostatic abnormalities consistent with or suggestive of increased fibrinolytic activity have been reported in a number of studies in children and adults with chronic cyanotic heart disease. However, whether and to what extent these abnormalities (increased fibrinogen/fibrin degradation products, decreased fibrinogen and euglobulin lysis time) reflect hyperfibrinolysis rather than impaired clotting factor synthesis by the hypoxic liver and impaired RES clearance of plasminogen activator and fibrin degradation products remains quite controversial [7, 8]. It appears that the hemostatic abnormalities seen in patients with chronic cyanotic heart disease are very similar to those observed in chronic, severe liver disease, in which the importance of disseminated intravascular coagulation and increased fibrinolysis is also a subject of continued debate [9]. I don't think there is published evidence to support the routine use of ϵ-aminocaproic acid in patients on cardiopulmonary bypass to prevent or control excessive bleeding, except perhaps in children with cyanotic heart disease. I have never used ϵ-aminocaproic acid in patients on cardiopulmonary bypass with excessive bleeding. Dr Harker might want to comment in regard to this question.

DR HARKER: I would just like to make the point that if you are measuring fibrinolytic activity primarily by measuring euglobulin lysis time, split product and plasminogen levels, and so on, you find that all of the fibrinolytic activity that you can measure in these patients is secondary to previous deposition of fibrin.

For example, during the initial operative procedure you will see detectable levels of degradation products go up, and as soon as you administer heparin they fall back to essentially zero throughout the period of bypass. The levels then go up again after you stop administering heparin, pointing out that if you prevent fibrin deposition, then the fibrinolysis doesn't occur.

In our experience in looking at these problems, we have never been able to find in a large number of patients evidence that fibrinolysis was really responsible for the bleeding problem or that ϵ-aminocaproic acid was helpful, so I would concur with Heinrich.

DR HILL: Don Hill, San Francisco.

If you walk through a hospital blood bank you always see that they have their platelet packs in continuous motion. When the platelets are transferred to the operating room, they sit on the anesthesiologist's table without motion. Is there a price that we are paying for this, or can you let them sit there for an hour or so without any worry?

DR HARKER: The hour or two is okay. If it is very much longer than that, then you begin to really pay the price.

DR HOLLERAN: My name is Holleran from Indianapolis.

Going back to the question of protamine, we have some very strong feelings about protamine brands, as does Eli Lilly Company from Indianapolis. We are currently running a study, but we believe that the Lilly protamine has been proved to our satisfaction to be far superior to some of the generic brands.

MODERATOR COPELAND: Thank you.

DR BORKON: Mike Borkon from Kansas City.

Would the panelists kindly discuss the impact of autotransfusion on subsequent development or lack of development of coagulopathies after bypass?

MODERATOR COPELAND: Bill, do you use the Cell Saver?

DR DEVRIES: We use the Cell Saver. We also use the autotransfusion unit in intensive care.

If it is getting to the point where you are having a lot of autotransfusion, 300 mL every couple of hours, then you're going too far and you have to go back to the operating room. But I have seen no incidence of increased coagulopathy with it and it does recycle some of that. I worry about sterility, though, and I worry about platelets and that sort of thing. I don't do it over a period of more than four or five hours in the postoperative period. Then I discontinue it. But I do do it for the period during which, if the patient is bleeding actively enough, you can use it and sometimes it will save the patient.

MODERATOR COPELAND: Let me just ask the audience in general.

I believe the Cell Saver is in general use throughout the United States—is that correct? Let's see a show of hands. Well, everybody uses the Cell Saver.

What about transfusion from the pleurovac or whatever, the chest drainage set, how about that? Not as many; about half.

I think that gives us some feeling for what is going on in that regard. Any other comments?

DR HARKER: Just to make a comment, when the patient is fully heparinized and you obtain blood out of the wound, it is unlikely that there will be substantial activation of the coagulation cascade. However, you will certainly have activated removal of the platelets in that blood, so you will enhance the thrombocytopenia because the heparin will not prevent that process.

With respect to protamine, in vitro you will find that protamine sulfate dissociates from heparin over the course of half an hour, whereas the chloride tends not to, but there are no good data that have been published to try to show those kinds of changes in vivo.

MODERATOR COPELAND: We will have one more question on this topic, then we will go on for a few minutes to the VADs.

DR HILL: Aaron Hill, Falls Church, Virginia.

One question about management of anticoagulation after the institution of left ventricular assistance. How do you manage anticoagulation after institution of left ventricular assistance, specifically, with the centrifugal pumps?

MODERATOR COPELAND: That is a perfect question because we're going right on to the discussion of centrifugal and pulsatile VADs and the first question I had to ask Dr Joist actually was, when do you start anticoagulation, what drugs do you use, and how do you manage patients on a centrifugal pump from the point of view of the coagulation system?

DR JOIST: Well, let me first make a brief statement as to the nature of the hemostatic alterations with VADs. Ventricular assist devices are usually used in patients who have been on prolonged bypass and cannot be weaned off. Thus, you have a situation where you see the most severe bleeding and very profound hemostatic alterations.

We have carried out detailed, sequential studies in 10 patients and found that the alterations observed during bypass before insertion of the VAD were usually compounded as soon as the VAD was in place [10]. The abnormal flow conditions introduced by the configuration of the device, the biomaterial surfaces with which the blood interacts, and possibly other factors and mechanisms may contribute to further activation of platelets and the blood coagulation system and thus aggravation of the preexisting hemostatic alterations [10]. In this situation it is particularly important that adequate levels of platelets and blood coagulation factors are rapidly achieved and maintained with early and vigorous infusion of platelet concentrates and fresh frozen plasma. I don't quarrel with surgeons who give ten units of platelets and three to four units of fresh frozen plasma to particular patients even if there is no massive bleeding at the time of the VAD insertion.

The question of when to start anticoagulation is a difficult one. The procedure that is generally followed at St. Louis University with centrifugal VADs is that after protamine reversal, the patient is observed for several hours. If the outflow from the chest tube is less than 100 mL/h over a period of two to three hours, full-dose heparin is started with the goal of maintaining the activated clotting time between 150 and 200 seconds. That corresponds roughly to 1.5 times the control for the aPTT. If the patient is judged to require the VAD for a more extended period of time, then at some point the decision is made (usually at about a week) to switch over to Coumadin to maintain the prothrombin time between 1.3 and 1.5 times the control.

It is not clear to me whether there are sufficient data from studies in humans to suggest that additional antithrombotic agents, such as intravenous or oral Persantine or dextran, are definitely helpful and indicated. However, those agents are given in many centers.

MODERATOR COPELAND: What about aspirin?

DR JOIST: Aspirin is not used in our institution. The evidence from in vitro and in vivo studies suggests that aspirin is a potent inhibitor of platelet function and therefore would have potential to inhibit platelet deposition on artificial surfaces. Aspirin interferes less effectively with the adherence of platelets to the artificial surfaces than with subsequent events—that is, platelet aggregation or platelet cohesion and platelet release. Aspirin of course would also be likely to induce or compound abnormal bleeding. Probably because of this and the fact that intravenous aspirin is not readily available, its use in patients with VADs has been limited. No controlled studies with aspirin in either patients on cardiopulmonary bypass or patients with a VAD have been reported.

DR HARKER: Certainly the continuous infusion of minimally effective heparin is a big plus here, and when you can start it depends in large measure on how well you have dealt with the hemostatic capability of the platelets. That certainly provides a significant measure of hemostatic competence in the immediate period. Thereafter there is no question that the artificial surfaces and the flow characteristics of these assist devices have a substantial effect in destroying platelets.

In a limited study performed together with Dr Dembitsky, we have shown that in a pulsatile assist device setting, that is, in steady state, there is a substantial shortening of platelet survival time down to about three days compared with the normal of ten days, despite continuous infusion of heparin and dipyridamole administration. That contrasts with a similar study carried out with him in patients with a steady state Jarvik heart replacement, where continuous infusion of heparin together with dipyridamole administration was associated with a normal platelet survival time. There may be quite a difference between those two studies. We obviously need a lot more data to find out what the universe really represents under these settings. I think the studies demonstrate that that assist device is a very thrombogenically active device.

MODERATOR COPELAND: Bill, would you wait longer than three hours to start full intravenous heparin dosage in this type of patient?

DR DeVRIES: I think the key really exists in the operating room. You have to work as quickly as you can to get the patient hemostatically competent. Once this is achieved you should get the patient into the recovery room and start him or her on heparin as quickly as possible. Our patients are given dipyridamole before operation, and if they have an atrial fibrillation on the total heart (or are in a similar type of situation) we may even try using heparin to prevent clottion. We don't reverse the heparin at the time of the operation, but we stop administration several hours before operation. We do the usual things during the operative period. But the two things that can really ruin these patients faster than anything I know of are bleeding and stroke. So we work very, very carefully to make sure the patient is hemostatically competent and does not bleed. Then we start the patient immediately on intravenous heparin, and we even put dipyridamole down the nasogastric tube.

As far as aspirin goes, every time we have administered aspirin to a patient, he or she has bled. We have had some evidence, though, that if you monitor the platelet Factor IV and the β-thromboglobulins in some of these patients, the platelets will start activating. At that time we might be tempted to add aspirin during the postoperative period.

We are also keeping our patients on heparin. We are not putting them on Coumadin anymore, because we believe that heparin is the best anticoagulant system we have. It allows you to regulate the coagulation if the patients develop nosebleeds or something like that, and if the transplant comes along, you can perform the transplantation a little more rapidly than when you have to push fresh frozen plasma into a patient who has received Coumadin.

We are also toying with the idea of intermittent heparin rather than continuous heparin in the postoperative period after about a week or so. We believe intermittent intramuscular or subcutaneous injections might afford some protection and also avoid the intravenous site, which can cause infection.

MODERATOR COPELAND: Now, all of these comments refer to the total artificial heart?

DR DeVRIES: Yes, the total heart or the bridge with the Symbion, that's right.

MODERATOR COPELAND: Let's go back to Dr Joist.

DR JOIST: I want to make one quick comment in regard to Dr Harker's remarks. We have looked at a limited number of patients who were on VADs for a prolonged period of time. In fact, we had 1 patient who was on the device for 91 days. Based on fairly extensive and detailed studies of blood coagulation and platelet function (accumulation in plasma of platelet specific proteins [βTG, PF4], platelet aggregation to adenosine 5'-diphosphate and other stimuli, fibrinopeptide A in plasma) in these patients, we were impressed with the fact that there was no detectable evidence of platelet activation at later stages, that is, at 60 days and 90 days, suggesting that once the patient is clinically stabilized, the VAD surfaces become passive or biocompatible. Thus, we could not detect any activation of either platelets or blood coagulation in these patients right before or very close to the time when they received transplants.

MODERATOR COPELAND: Okay, let's go on to the pulsatile VADs. Do they require anticoagulants?

DR JOIST: The scheme with pulsatile VADs that is currently used at St. Louis University is that patients are not routinely started on heparin immediately, but are given dextran. The reason is that the incidence of thromboembolic complications seems to be less with these devices than with the centrifugal devices. If the patient needs to be on a pulsatile device for a longer period of time, the patient is started on either heparin or Coumadin. At the time oral anticoagulation is started the patient may also be switched from intravenous dextran to oral Persantine.

MODERATOR COPELAND: Are patients placed on heparin during weaning in these pulsatile devices?

DR JOIST: Yes.

DR HARKER: I would like to argue that the pulsatile devices are not different than the total heart in concept, in that they require the same antithrombotic approach as would a Jarvik artificial heart. You should use anticoagulation and dipyridamole, given our current understanding. It is very clear that you can get demonstrated platelet consumption in those settings. I think that is indicative that something is going on.

MODERATOR COPELAND: Our own approach has been influenced by thoughts about what happens to the cannulas in the left atrium and the aorta in the absence of anticoagulation, and therefore we also have tended to follow that policy of giving heparin to patients with the pulsatile VADs.

Let's go on to any discussion or questions from the audience on the area of VADs, centrifugal or pulsatile. We have time for perhaps one or two comments or questions.

DR PENNINGTON: Glenn Pennington, St. Louis.

I agree with Dr Harker that the pulsatile assist devices are certainly very similar to the total artificial heart because they have prosthetic valves and they are obviously made of similar biomaterials. I think the difference is that in a patient who might have myocardial recovery the time is much shorter, and therefore the length of time for developing a thrombus is much less. Indeed we have had many patients carried through that regimen with dextran only who have absolutely no evidence of clot or thrombus in the pump, valves, or tubing. However, once the patient has been on the VAD for about a week—and understand, we have supported patients for as many as 75 days on ventricular external pulsatile devices—we become concerned. At that point I certainly agree with you that we need some type of anticoagulation. I think in the short term, however, we certainly have shown that anticoagulation is not essential. We believe that eliminating anticoagulation is a very important factor in having patients survive. Once you take heparin out of the mix, you greatly simplify your bypass procedure.

MODERATOR COPELAND: Glenn, what is your dextran dosage?

DR PENNINGTON: It is 25 mL/h of the 5% dextran.

MODERATOR COPELAND: Thanks.

DR WAGONER: Phil Wagoner from Indianapolis.

What is the best way to monitor your anticoagulation status during a bad run? We found that if we maintain an elevated PT/PTT system but the ATT level starts dropping, then we are running the risk of thromboembolism, but at the same time the PTT value starts getting way up there and then our patients start bleeding. So I think at bedside we're tempted to just run strictly by the activated coagulation time, but sometimes we find ourselves maybe going back to surgery because of bleeding.

In your opinion, what is the best monitoring tool?

MODERATOR COPELAND: Okay, I am going to ask each panelist just to say what test they think is the best.

We use the PTT, which we keep elevated at one and a half to two times control values. Bill?

DR DeVRIES: The same thing, PTT.

MODERATOR COPELAND: Laury?

DR HARKER: Partial thromboplastin time.

MODERATOR COPELAND: Heinrich?

DR JOIST: We use the activated coagulation time as well as the aPTT. The time required for turnaround of the results obviously is an important consideration, and I have a difficult time guaranteeing a turnaround of the aPTT results in less than 30 to 45 minutes. That is probably the main reason why we use the activated coagulation time in the operating room as well as the aPTT.

DR HARKER: I believe the reason that Dr Pennington is enjoying protection is obviously because he is using dextran. Dextran certainly affects platelet function and fibrin formation. So whether one uses that temporarily or something else, I think you get the same benefit of having some kind of antithrombotic therapy.

MODERATOR COPELAND: Okay. Finally, we are going to go on to discuss just for a couple of minutes the total artificial heart, which for practical purposes in the world experience means the Jarvik-7 or Jarvik-70. The question that is the most important, at least in my mind, is whether thrombosis is inevitable in the Jarvik heart, and if so, when it occurs and how you detect and prevent it.

First, let me just say that in our own experience with the current models of the devices that are available, we have seen fibrin deposits in the crevices around the valve mounts in every valve in every single patient. It is our belief, therefore, that tiny amounts of fibrinous deposits are pretty much inevitable in the face of therapeutic anticoagulation, and that as a consequence of these there is a risk of small cerebral events, transient ischemic attacks, tiny strokes, and small neurological events, but without sequellae.

On the other hand, our experience with 1 long-term patient is that when what we believed was endocarditis developed in the device, a larger embolus occurred with a more massive amount of cerebral damage.

So, that has led to our philosophy of not putting the Jarvik device into anyone who is going to need a device for more than 3 weeks and of transplanting as soon as we can in a bridge to transplantation situation, providing the patient is a reasonable candidate for transplantation.

Now, I'm sure that Dr DeVries has a slightly different point of view. Bill, what are your thoughts?

DR DeVRIES: I think when you start talking about thromboembolism, you are really talking about many, many things and they all have an effect. Any time you put a foreign body in contact with the blood you are going to have surface activation, and you have to expect that you are going to have thromboembolism.

I think it is directly related to many factors, though. I think it is related, as you say, to the flow pattern, the distribution about the valves. I think it is directly related to the time that you keep the device in. The longer the time, the greater chance of thromboembolism.

It is related to the patterns of flow. I know you run the heart a little bit faster and say that that will decrease the chance of thromboembolism, and I think that that is a reasonable thing to say.

It is also related to the level of dehydration and patient factors such as infection. There is no question that infection of these prostheses is a problem. It will release coagulants and cause anticoagulant problems. For that reason I think it is absolutely critical that we keep these patients as free of infection as we possibly can, whether we are talking about a period of four days or 2 years. As we get into the longer runs, say over 30 days, we have been able to keep four permanent hearts fairly free of infection and to use a decreased amount of stroke during that period of time. I think if you are going to go longer than 30 days, you really have to worry about infection inducing thrombosis, and that's the key. I think in this type of patient you just have to be sure that your anticoagulant scheme is well monitored and kept adequately at all times, that it doesn't drop down at 2:30 in the morning or something like that. You really have to work on the infection, however, because at that point infection becomes the critical limiting factor of the whole process.

Also, as you say, frequently the stroke will signal the fact that the patient has a bout of endocarditis. If you look at the thrombus in many of these patients with long-term devices you will see bacteria in the thrombus at that time. You are asking whether thrombus came first or the bacteria came first, and that's a good question. There is really no way to answer that.

MODERATOR COPELAND: One thing I might say about the total device is that it would appear that the segmented polyurethanes are generally free of deposition of thrombus, which has been a very nice experience for us.

Let me ask our two hematologists here—we are almost to the end and we want to get a few quick comments from them—what is the optimal anticoagulant regimen for these total artificial hearts. What drugs would you use?

DR HARKER: Of the available drugs that can be used clinically, the regimen that has proved most successful and has the most rationale is continuous infusion of heparin in addition to dipyridamole administration.

When, however, there is infection, tissue factor production by mononuclear leukocytes is resistant to both of those agents, and I think that explains the dilemmas that one has then.

MODERATOR COPELAND: Heinrich?

DR JOIST: I agree with Dr Harker. It seems to me that one ought to use as powerful an antithrombotic regimen as possible and necessary under the circumstances, as the thromboembolic complications frequently are devastating and permanently disabling, whereas excessive bleeding that might occur as a result of or be aggravated by the antithrombotic drugs can usually be controlled. But I don't know what the most efficacious antithrombotic regimen in patients with VADs or the total artificial heart is.

MODERATOR COPELAND: It looks like we still have a few things to learn about this area. I thank the panel very much and also thank the audience for their participation.

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Panel 4

Other Postoperative Complications

Moderator: William S. Pierce, MD
Panelists: Laman A. Gray, Jr, MD, Lawrence R. McBride, MD, and O. Howard Frazier, MD

MODERATOR PIERCE: We have here a panel of three members and myself, and I think we have all seen our share of problems and complications from the devices that we are talking about today.

I would like to introduce the panel members: Dr Larry McBride, assistant professor of Surgery at St. Louis University; Dr Laman Gray, professor and chairman of the Department of Cardiac Surgery at the University of Louisville; and Dr Bud Frazier, professor of Surgery at the University of Texas at Houston and chief of the Transplant Program at the Texas Heart Institute.

I would like to start off by saying first that our goal in the area of mechanical circulatory support is to prevent problems and complications. Sometimes when one gets into these problems and complications, it is simply not possible to get out of them in good fashion. Our goal, therefore, has to be to prevent these problems.

By far the biggest problem that occurs in patients that have these devices, in my experience—and I think most people would agree with this—is bleeding. The problem is of such severity that, of course, the previous panel was devoted to that subject. We want to keep that in mind, and what we are going to talk about are other and in some ways lesser complications than bleeding.

I would like to list what I consider to be six more or less generic problems that occur in patients on these devices. The first problem is that of an inadequate cardiac output in a patient who has a circulatory assist device in place. This problem may be very simple, that of hypovolemia; in this case, both atrial pressures are low and the cardiac index is less than 2 L/min/m^2. We would try to improve the cardiac index by increasing the patient's blood volume.

Another scenario is that of a patient who has a high left atrial pressure and a left ventricular assist device (VAD) that is not functioning properly. Well, the problem in that instance is some type of cannula obstruction. The surgeon has to look at that to find out what it is, reposition the cannula, and get the left atrial pressure down.

The next scenario is that of a patient with an inadequate cardiac output in spite of a left VAD that seems to be functioning satisfactorily. There is a low left atrial pressure, and no one seems to be able to understand what the problem is. Well, the problem is that the patient has concomitant right ventricular failure that may have been unmasked by the insertion of the left VAD. What one has to do then is to get more blood over to the left side of the heart. At the operating table you may be able to do it for a few beats simply by massaging the heart, and all of a sudden the person who is watching the drive unit says, "Oh, the pump is filling and emptying very nicely; what in the world did you do?" When you stop massaging, things go back to their former state. That is a very hard-core definition of right ventricular failure. It's a real problem. It occurs somewhere in the range of 50% of patients who have left VADs in place, and you have to have a plan to treat that or you're going to be faced with a patient with an inadequate cardiac output, and then other problems will ensue.

Another problem that has occurred in a few instances has been shunting. In a patient who has a left VAD and a high right atrial pressure, there may be a patent foramen ovale that had otherwise not been of any importance. All of a sudden the arterial blood is desaturated; the PO_2s may be very low. The problem in that instance is related to the significant disparity in the two atrial pressures in the presence of what had previously been an insignificant patent foramen ovale.

Hemolysis occurs in some of these patients. The assist devices have all been checked out in laboratory bench and animal studies and hemolysis does not seem to be a problem, but in the patient who has been on cardiopulmonary bypass for a period of time—and apparently some patients have different osmotic fragilities or mechanical fragilities of their red blood cells—we do on occasion see hemolysis. It does not appear to be related more to one device than another; it has occurred with a variety of devices.

End-organ failure is another important complication. In such a case you have to determine if the end-organ failure was related to the delay in the therapeutic procedure. When a patient goes to the cardiac catheterization laboratory with low blood pressure and cardiogenic shock, everything from that point on may be done absolutely perfectly, but that patient may end up with end-organ failure. The problem may occur after cardiopulmonary bypass, where a prolonged time is spent administering a variety of inotropic drugs and letting the patient sit with an inadequate cardiac output. Again, end-organ failure will result regardless of what assist device is put in and how nicely it functions. And finally, if the assist device does not have an adequate output, the patient will end up with end-organ dysfunction.

Device failure is another complication. Fortunately, it is not common, but we are aware of fractured valves, tubing and roller pumps that can split, and drive-unit failures. One has to be aware of those problems and be able to

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make diagnoses promptly and take the appropriate measures.

The last complication I want to mention is the problem of infection. I'm not talking about infection that causes problems within the first 48 hours. After that period of time, however, when a patient has fever and things aren't going well, one certainly has to consider the problem of infection. One of the things that we have been doing, and I know other groups have also, is trying to improve the nutrition in these patients as quickly as possible. Start to get some calories on board as an aid to preventing long-term infection in a patient who is going to be on one of these devices for a period of time.

I have asked each of our panelists to give a brief presentation, first of all to tell us which particular device they have been involved with and then to tell us a little bit about what some of the complications have been and how they have modified their work in an attempt to prevent these problems in the future. Dr Laman Gray will give the first presentation.

DR GRAY: Thank you very much. I think it is important for everybody who is not working with these devices to understand that there are many devices on the market as well as different uses for the various devices.

The device I am going to talk about is the Thoratec/Pierce–Donachy VAD, which can be used after cardiotomy and as a bridge to transplantation. However, I am going to limit my discussion to a very specific subset of patients with complications that are somewhat different, and the use of the device as a bridge to transplantation.

One of our interests has been in the use of the Thoratec/Pierce–Donachy heart as a bridge to transplantation. This is a pure series of patients; there are absolutely no patients who were put in this group after cardiotomy and converted either into or out of the series.

We implanted the VAD in patients who we believed were candidates for cardiac transplantation and who deteriorated to the point (by the criteria talked about earlier today) of cardiogenic shock.

Three patients died immediately before we considered transplantation. I will discuss these deaths in just a minute. The 6 remaining patients underwent cardiac transplantation. Five of the 6 patients are home, alive and well. The minimum follow-up right now is 6 months. The longest follow-up is 3 years after biventricular assist.

One patient died immediately after cardiac transplantation, and I will dwell on that because that is the first complication we had. That complication was most probably an error in judgment. The patient was a 15-year-old boy who went into cardiogenic shock. We implanted a left VAD, and the patient developed a coagulopathy and had significant bleeding. Unfortunately, at the same time that the device was being implanted, a heart was found and the decision was made to go ahead and perform transplantation.

The patient had been on the assist device for about 12 hours when he underwent the orthotopic transplantation. The combination of having insertion of the VAD where he had a coagulopathy, which had actually come under control, and being put back on cardiopulmonary bypass and having the transplantation resulted in the development of another coagulopathy, disseminated intravascular coagulation. The boy died about 24 hours after the cardiac transplantation from bleeding problems and associated pulmonary problems.

I think the first thing we have learned is that these devices, as you will see, are safe. I think it is better to put the device in and stabilize the patient before proceeding to transplantation. It is much better to have the patient stabilized than to proceed with a transplantation on an emergency basis.

Our patients varied in age from 14 to about 55 years. The group who died were neither the oldest nor the youngest. The most common indication for transplantation was idiopathic. There was 1 case of postpartum cardiomyopathy, and 1 case of ischemic cardiomyopathy, which I will mention in one minute.

In one of the patients who died, we were performing a reoperation as the patient had previously undergone bypass operation. He came back with an ejection fraction of approximately 10%. We did not deem him feasible for repeat coronary bypass operation and he was placed on the network for elective heart transplantation.

His condition deteriorated and we put in the VAD. He had a massive bleeding problem secondary to all the adhesions in the pericardiac cavity. The patient developed disseminated intravascular coagulation and died in about 24 hours.

The decision as to whether to put in a right ventricular, a left ventricular, or a biventricular assist device has to be left to the operator. My supposition when we started the series was that virtually everybody with cardiomyopathies needed biventricular assist for bridging to transplantation. However, we quickly found out that when we put in the left VAD and the patient did well, left ventricular assist was enough. In our series, approximately 50% of the patients required biventricular assist and 50% required only left ventricular assist.

This decision is critical, because if you misjudge and just put in a left VAD, 12 hours later you may have to put in the right VAD, which can be a problem and cause a death if you have to put the patient back on bypass to insert the assist device.

There are some basic criteria for deciding when to put in a right VAD. The first question is: does the right heart distend when you look at it? Is it functioning well?

The second question is whether you have increased right atrial pressures. You can tell by measuring directly or filling the atrium.

The third thing, which I think is very important and refers to what Bill was talking about, is that to help minimize complications in all these patients, it is extremely important to monitor them properly.

For all patients who have had the Pierce–Donachy device inserted, I think all senior investigators use direct left atrial lines to measure the left atrial pressure. So if you see a patient, as Bill has mentioned, who has low left atrial filling pressures and distention of the right heart, that patient has high right atrial pressures, and you know immediately you have to put in a right VAD.

Major complications that we had in the group included renal failure that already existed before insertion of the VAD. The young boy in this case had a biventricular assist device placed. He then underwent hemodialysis while on the VAD, underwent cardiac transplantation, and continued hemodialysis, and his kidney function returned to normal. He is home leading a normal life at this time.

The biggest problem was bleeding, which caused 3 patient deaths. The fourth patient, who died after the heart transplantation, also had bleeding. One bleeding problem was a technical problem associated with the cannula. The other bleeding problems were related to coagulopathies.

Bleeding problems led to "shock lung" and multiorgan failure, and to pulmonary failure secondary to massive transfusions (for example, 30 units of blood given trying to control the coagulation problem). These are common findings in these patients.

There is no question that you can maintain an adequate flow in the VADs. This had no relationship to death because the flows were adequate in all of our patients.

Three patients, as I mentioned, died on the VAD, one after the transplantation. Again, all deaths resulted from bleeding leading to pulmonary insufficiency and then multiorgan failure. The interesting thing about this is that in the 3 patients who died on the VAD, there was never any question about whether they would become candidates for transplantation. It became clear very early in the postoperative period that they would not be stabilized and would not survive.

To give you an idea of what type of bleeding we are talking about, I will discuss just a few of the patients. In patients who did all right and were bridged, we had moderate output from the chest tubes. Three thousand milliliters per minute is high, but the patients with the coagulopathies had outputs of 8,000 mL/min. These were massive coagulopathies. Most of these patients had been returned to the operating room at one time or another, and the bleeding could not be stopped. They were all being evaluated by our hematology service, and had all possible replacement of all blood products.

It is our feeling that coagulopathy secondary to large amounts of transfusions leads to pulmonary hypertension and then to inability to fill the left VAD. As a matter of fact, 1 of the patients who did have pulmonary hypertension before insertion of the VAD had a right heart systolic pressure of around 130 mm Hg and a direct left atrial pressure of 0, so the blood could not get through the lungs.

Fixed pulmonary hypertension is a contraindication to performing a VAD implantation if you want to do it as a bridge to transplantation. I think this is the same as for cardiac transplantation. I do not mean to say, by any means, not to insert a VAD in people who have pulmonary hypertension; they just are going to have fixed pulmonary hypertension.

There was an infection in 1 patient, a pneumonia caused by Legionnaire's disease; this occurred three or four days after insertion of the VAD. The patient was taken off the cardiac transplant network and the Legionnaire's disease was treated. This resolved, and transplantation was successfully performed. We had no VAD-related infections in any of the patients.

One patient had hemolysis, which was easily controlled. Two patients had renal failure, both preexisting renal failure. One patient's renal failure totally cleared during ventricular assist; the other patient required hemodialysis.

There were no neurological complications and no renal, hepatic, or pulmonary complications outside of the bleeding problems that I mentioned. It is also interesting that if you have biventricular assist in patients with preoperative pulmonary edema, it is very easy in manipulating the outputs from the two devices to get the pulmonary edema to resolve.

There were no device-related problems. We had no mechanical failures or VAD console failures. There was one cannula-related problem, and we had no embolic problems.

MODERATOR PIERCE: Thank you very much, Laman. I'm sure there will be questions generated from that series, which was a rather pure one in using one particular system.

There is nothing that Dr Pennington and I like more than to see a young cardiac surgeon who gets interested in this general area, and our next speaker from St. Louis University, Dr McBride, is just such a young man. He is going to tell us about complications that have been seen in the St. Louis program.

DR McBRIDE: Thank you, Dr Pierce. The group that I am going to be talking about is a group of patients that we have supported at St. Louis University for more than 21 days with a VAD, a pulsatile device.

We have had 6 men and 1 woman who were supported for greater than 21 days; their ages ranged from 28 to 56 years. Their duration of support ranged from 23 to 91 days. Four of the patients had isolated left VADs and 3 of them had biventricular assist devices. Six of the patients were supported with Pierce–Donachy/Thoratec pumps, and 1 patient was supported by a Novacor device for 91 days.

In all of these patients we were able to establish hemodynamic stability. Six of the patients were cannulated through the left ventricular apex in anticipation that their heart would not recover. One patient, in whom we weren't sure what the ventricle was going to do, was cannulated through the left atrial appendage.

Of this group of patients, 4 have undergone successful transplantation. One patient was just transplanted 48 hours ago, so we hope to have 3 long-term survivors.

One patient died 6 months after transplantation of noncompliance with his immunosuppression regimen. Three patients could not undergo transplantation because they developed multiorgan failure, which contraindicated transplantation.

Among our most common complications in this particular group, bleeding, which is commonly reported in our larger series as at other institutions, occurred in only 2 patients. They both required reexploration, but there were no sequelae from this.

Our most common complication was infection. All 7 of these patients had some type of septic process during their period of support. The most common problem was pneumonia, which occurred in 4 patients, 3 of whom died. We saw 1 episode of mediastinitis early in our experience in a patient in whom we initially inserted a Thoratec left VAD. Approximately 12 hours later we inserted a right Bio-Medicus pump, which was removed five days later after the right heart recovered, but mediastinitis developed.

We have had several device-related infections ranging from an infected Novacor pocket, which we were able to treat with systemic antibiotics and local debridement (this was in the patient who underwent transplantation 48 hours ago), to local infections around the cannula sites. Our policy for those types of infections has been to try to debride the area as gingerly as possible and to administer systemic antibiotics. In general, we have been successful in handling these local cannula infections.

We have had 3 patients who had evidence of thrombus formation. In 1 patient thrombus was found in the cones of the Bio-Medicus pump. Two of the other patients had Thoratec pumps, and 1 developed a cerebral embolism after the pump malfunctioned. Before that time, while the pump was functioning well, he had no problems at all. The other patient had multiple organ failure and did not survive. On postmortem examination she had evidence of microemboli to her brain and kidneys.

Renal failure occurred in 2 patients, both of whom required hemodialysis. Neither of these patients survived. In our larger series of postcardiotomy patients, the presence of renal failure was an important prognosticator of survival. Eighty-six percent of our nonsurvivors of postcardiotomy support required dialysis, so this is a real problem.

We have seen one episode of pump failure; fortunately, that patient did go on to receive a transplant and survived. We saw one episode of significant hemolysis as defined by an elevated free serum hemoglobin level of greater than 40 g/dL. This was not a clinical problem, and the patient did well.

Regarding the problem of infection, it's clear that all of these patients have a profound T-cell lymphopenia during the perioperative period when the device is inserted, and this is most marked at about 48 hours. Fortunately, with time, if the patients remain hemodynamically stable their T cells will return to normal levels, even with the device in place. The biggest determinant of T-cell activity is whether or not the patient develops multiple organ failure.

The presence of infection appears to be related to the duration of support. If you take a look at our postcardiotomy patients who were studied retrospectively, those patients who were only supported for a mean of 24 to 48 hours did not have any significant episodes of sepsis. Those patients who were supported for three to 21 days had an incidence of infection of approximately 70%. The presence of infection did portend poor survival; 70% of postcardiotomy patients who were not infected survived, whereas only 30% of the patients who had infection survived.

MODERATOR PIERCE: Thank you very much, Larry. We appreciate your sharing that series with us. Our final panelist of this session is Dr Bud Frazier, who has had experience with several different types of devices at the Texas Heart Institute.

DR FRAZIER: "Other" is always a great subject to address. It reminds me of a story that Dr Cooley tells about the early days of congenital heart surgery. In the early 1960s, a nationwide convention was held to focus on follow-up for pediatric heart patients. At that conference, Dr Cooley suggested a simple patient classification of "alive," "dead," and "other." So today, in terms of postoperative complications, we're going to discuss "other," a term that, I think, allows for a lot of leeway.

We have used several types of blood pumps at the Texas Heart Institute. We used the Jarvik pump to support a patient for 31 days and he is now alive and well 2 years after transplantation. We are initiating experience with two other pumps that we hope will be placed on the market soon.

I am not going to discuss in detail the Bio-Medicus centrifugal pump because it will be the focus of discussion later in this conference. However, it is the pump that we use most often because it is a simple device that is both readily available and inexpensive. Within the past year, we have used this pump in 2 cases of right heart failure after transplantation.

I think the main cause of right heart failure is pulmonary resistance, which is just too high and usually involves some spasm (although that can be treated). As Dr Gray has alluded to, pulmonary resistance may be complicated by transfusions. Both of our patients could not be weaned from cardiopulmonary bypass and thus were placed on the right VAD, 1 for 48 hours and 1 for 72 hours. In both cases, after removal of the device, heart function was normal.

In postcardiotomy patients who can't be weaned from bypass, I prefer to cannulate through the ventricle itself. With this technique of right ventricular cannulation, an effective pursestring suture can be placed around the right ventricle and the pumps can actually be put in place with the heart beating.

Similarly, with left ventricular assist, I have found that a simpler way to perform cannulation is to revert to the old design, placing a pursestring suture directly into the left ventricle for left atrial return, and then going through the aortic valve, positioning the cannula by the arch for the return. This technique is helpful because it allows the surgeon to easily close the sternum and bring the cannulas out underneath the costal margin (as with a chest tube). Also, I believe that this procedure is well tolerated by the patient.

There has been some concern over the size of blood pumps. We were able to use the Bio-Medicus centrifugal force pump in a 9-year-old boy. Despite his small size, the child was supported for 14 hours with this device with essentially no cardiac function and a nonpulsatile flow (as no intraaortic balloon was inserted). He later underwent successful transplantation, and is doing well after 6 months.

Another complication that, I think, is important to consider is fungal infection, which occurs in our immune suppressed patients. Any patients who have had these devices are going to be immune suppressed. Through M.D. Anderson Hospital, we have had access to a new drug for treatment of these infections. The drug, liposomal amphotericinol, was developed by an Anderson staff physician, Dr. Gabriel Lopez Berestein. It is a form of amphotericin that is transmitted in a liposomal bilipid carrier. E.R. Squibb & Sons will begin distributing the drug later this year, and it is hoped that it will be commercially available soon.

The main advantage to this remarkable drug is that it can be administered in enormous doses with no nephrotoxicity. We gave 8 g of the drug over a 30-day period to our patient on the Jarvik device after he developed a fungal pseudoaneurysm of the ascending aorta. Thus, I believe the drug will be of great help to us as it becomes generally available, particularly in the treatment of candidiasis.

We have also had 2 patients with disseminated aspergillus that we were able to treat with this drug. Both of those patients are survivors.

Although we are still on the fringes of development of circulatory support devices, I believe we are beginning to see some real therapeutic results from our efforts.

MODERATOR PIERCE: Thank you very much, Bud. I would now like to open this session to the audience and ask if there are any questions regarding what we are glibly calling "other" complications, a wastebasket of complications.

While questions are being thought of, I would like to see how the panelists feel about the use of hemodialysis in a patient who is on some type of an assist device. Bud, could you comment about that? Have you had experience with it and do you have a feeling for it?

DR FRAZIER: Hemofiltration has been incorporated in all of our patients on circulatory support. In the majority of patients who are weaned from support, there is fluid imbalance and other fluid problems. The more you can decrease the excess fluid, the better your chances are of decreasing all of these pulmonary complications.

MODERATOR PIERCE: Laman, do you have any experience?

DR GRAY: We have had experience with 1 patient who required hemodialysis immediately after insertion of the VAD because he had a potassium level of 17 mmol/L. Obviously he was in asystole, and we put him on hemodialysis using a Shiley catheter through the subclavian vein. We were able to get his potassium level down to more normal levels in eight hours, and he then converted back to a normal rhythm.

MODERATOR PIERCE: Thank you very much. Larry?

DR McBRIDE: At St. Louis University, all patients who have been on supportive devices and have required hemodialysis have died. We haven't had any survivors of that.

We have used intraoperative ultrafiltration when the patient was overloaded with fluid before insertion of the assist device and we found that to be useful, although we removed a couple of liters of fluid during the procedure.

MODERATOR PIERCE: We had 1 patient that had a total artificial heart in place and required hemodialysis for 40 days; at that time kidney function seemingly miraculously returned, and that patient ended up with a creatinine level in the range of 1.5 mg/dL and did not need subsequent hemodialysis. So, hemodialysis certainly can be an effective treatment modality.

We have a question from the floor.

DR TYRAS: Tyras from New York. I would like to poll the panelists. In patients receiving the assist device, what antibiotic regimen do you use while the assist device is in place? Also, is this different in the postcardiotomy cohort of patients compared with those who have the assist device as a bridge to transplantation?

DR McBRIDE: If our patient does not have active infection before insertion of the device and he has been in the hospital fewer than five days, we use cephalosporin antibiotics. Our intent is to use them for approximately three days, at which time they are discontinued. If the patient has been in the hospital for more than five days, we use a cephalosporin and also an immunoglycoside, because of a high incidence of gram-negative colonization in our intensive care units. Again, if there is not an active preoperative infection, we will discontinue antibiotic administration after about three days.

If we have a patient that has an ongoing infection and we elect to go ahead and support this patient—although we look at these patients very closely—we would continue administration of the antibiotics that the patient is already on, and would add whichever antibiotic would be appropriate for preventing *Staphylococcus* infection.

DR GRAY: We do exactly the same thing. We don't really treat such patients any different than routine transplant patients.

DR FRAZIER: We do basically the same thing with a cephalosporin until we have a specific infection to treat. Our infectious disease consultants prefer to administer a small dose of amphotericin if they see any sign of change in the fungal titers.

DR BRONSTEIN: Bronstein, Daly City. My question is for Dr Gray. I noted that you had no infections, and I wanted to compliment you. I wonder, however, do you take any special precautions in the intensive care unit in patients who have a long-term left ventricular assist?

DR GRAY: The only real precaution we have been taking in the intensive care unit is keeping Betadine-soaked sponges around the tracts where the tubes go under the skin. Besides that, we use a mask and some gloves, but really nothing exceptional. We do not go into a full reverse isolation or anything.

DR FRIST: Frist, Vanderbilt, Nashville. My question centers on an issue that Dr Pierce mentioned, that of the patent foramen ovale. Dr Gray, you also mentioned the transient increases in pulmonary vascular resistance that are seen with either very long pump runs or infusion of a lot of blood products.

We used a Novacor left VAD in a patient for 33 days. In the first two days we clearly opened the patent foramen ovale, which caused a great deal of difficulty in patient management. Pharmacologically we were able to manage that patient and perform a successful bridge to transplantation.

My question is, should we routinely look for and close the patent foramen, or should we just look at those patients who have a long pump run or those patients in whom we have infused a lot of blood products? This is with regard to the use of the left VAD alone.

MODERATOR PIERCE: We have had 2 patients in our series whose deaths appeared to be intimately related to an inability to oxygenate blood and shunting across an unsuspected patent foramen ovale. As a result, if we are going to put a left ventricular assist pump in a patient, we digitally explore the right atrium and see if we can feel a patent foramen. If we can, then we use bicaval cannulation and open the atrium and put a couple of stitches through that flap.

Any comments about the patent foramen?

DR FRAZIER: Well, it is an interesting problem. We recently had a patient on left ventricular assistance whose cardiac function would improve as his condition improved. When we would try to wean him back, the right-sided pressures, I suppose, increased. At that point we would see desaturation occur, and the patient couldn't be weaned. Finally we had to take him back to the operating room, and instead of opening the atrium, we inserted a right-sided pump, which seemed to work effectively.

DR GRAY: We do exactly what Bill does with the patent foramen. Certainly we have had some problems with the foramen, and I think it is something to be aware of. In our experience, however, the administration of prostaglandin E_2 directly into the pulmonary artery has saved many patients who had pulmonary hypertension.

DR PENNINGTON: Device failure was mentioned earlier as an occasional problem. When we started in this business, we always had a technician at the bedside 24 hours a day. Now we have patients on these pumps for 75 to 90 days and, frankly, there's no technician there anymore. I wonder if we could get an assessment on this from the panel.

MODERATOR PIERCE: Do you have a technician sit there at the bedside, Bud?

DR FRAZIER: No.

DR GRAY: No.

DR McBRIDE: No.

MODERATOR PIERCE: We do not do that, either.

Thank you very much. We are going to end this session. I appreciate your interest and participation.

Panel 5

Weaning and Bridging

Moderator: George J. Magovern, MD
Panelists: Leonard A. R. Golding, MD, Philip E. Oyer, MD, and Christian Cabrol, MD

After a patient has been supported with a circulatory assist device, the expected outcomes are weaning, bridging, or discontinuation of the support. An early insertion of the device will avoid deterioration of the heart and other organs to an irreversible condition. Cardiac assistance for a minimum of 24 hours is recommended with a mild dose of anticoagulant. It is necessary to monitor the hemodynamic functions during circulatory support and weaning. Most of the mechanical devices are quite reliable, and complications during ventricular assist are easily managed. The patient should be in the same condition as an ordinary elective transplant candidate before transplantation. Patients with an artificial heart or ventricular assist device should not be on the priority emergency list for cardiac transplantation. Patients suffering from cardiogenic shock can be stabilized with a ventricular assist device to allow the heart to recover or be provided with other treatment. A circulatory support device can also be used as a bridge for patients awaiting a cardiac transplant.

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DR L. A. R. GOLDING (Cleveland, Ohio): Most of our experience has been with the centrifugal pump, originally the Medtronic and now the Bio-Medicus pump. It is desirable to reach a point of being able to wean the patient when the heart is recovered; however, at times it will be done much sooner because of a hopeless situation.

Is there a minimum time to support these patients? Our experience suggests that if you have enough reason to put in one of the devices, you should leave it in for at least 24 hours once it is placed. We had some hard early experiences with a couple of right ventricular assist devices in the early days; when the patients were rapidly weaned once they looked good in less than 24 hours, calamity resulted. We suggest that once a cardiac assist device is employed, certainly for postcardiotomy use, it should be left alone for at least 24 hours. Hopefully, the patients will be stabilized during that period.

How do you decide whether it is time to wean? It is based on hemodynamic monitoring. A left atrial catheter and a Swan–Ganz catheter are normally inserted. Another simple aid is to watch the arterial tracing to see the improved ventricular output by turning off the balloon. With a centrifugal pump the ejection can be easily identified and the Swan–Ganz cardiac output measured. At the same time, left atrial pressure should not be substantially increased. As pump flow decreases, the cardiac output measured by thermodilution should be maintained if the cardiac function is recovered. The blood flow should be at least 2.2 L/min/m^2, with a higher flow range desired.

The centrifugal-type devices have the characteristic that they cannot be run at a flow rate much below 0.5 L/min. It is advisable to maintain the activated clotting time at about 1.5 times normal while providing support with the assist device. When pumps are at the lower flow states during weaning, it is appropriate to increase the heparin dosage to minimize the potential of deposition.

The patient should be weaned to the intraaortic balloon pump and mild cardiotonic support. It certainly makes sense to infuse a small dose of dopamine or dobutamine at this final weaning stage for the renal function. Most of the postcardiotomy patients who require ventricular assist have a balloon pump. It is believed that the balloon pump should be left in place for 24 hours after the removal of the ventricular assist device. Decannulation itself, at least the way we have done it, is not a big problem. We leave pre-placed pursestring buttress sutures on tourniquets, and they are actually inside the chest.

The survivors who required ventricular assist have the following common characteristics:

1. They have fewer than 75 hours of pump support.
2. Their right ventricular failure is mild or absent.
3. They have some left ventricular function recovered within 24 hours.
4. They have no evidence on electrocardiogram of postoperative myocardial infarction.

In addition, 1 patient with an implantable left ventricular assist device is still continuing to do well with the pump support at 150 days.

Table 1 shows a list of patients who received the Bio-Pump for single left-sided support as a bridge to transplantation during the last 2 years. They were grouped into nonsurvivors and survivors; the success rate is 50%. Patient 4 (B.R.) had a mitral valve replacement and was unable to be separated from cardiopulmonary bypass. During the early stage of left ventricular assist, a decision was made that the heart would not recover. A successful cardiac transplantation was performed with a good outcome. Pathological evaluation revealed foreign body microemboli of an unknown source in the native

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Table 1. Cardiac Transplantation Using the Bio-Pump Left Ventricular Assist Device as a Bridge

Patient	Age (yr)	Duration (days)	Transplantation	Survival
W.S.	34	5	No	No
K.K.	44	9	No	No
L.N.	43	15	No	No
B.R.[a]	56	2.5	Yes	Yes
J.B.	50	3	Yes	Yes
D.L.	23	31	Yes	Yes

[a] This patient received the Bio-Pump after a mitral valve replacement and failure to be weaned from bypass. The indication for use of the Bio-Pump in all other patients was as a bridge to transplantation.

heart, which supported our clinical decision of transplantation.

The last patient (D.L.) was a 23-year-old man who was supported by the Bio-Pump for 31 days before heart transplantation. The pump head was replaced three times during the ventricular assist, with clear indications that two of the pump heads needed to be replaced. This result suggests that when a more sophisticated device is not available, the Bio-Pump can be used to support a patient's circulation for at least 1 month.

DR G. J. MAGOVERN (Pittsburgh, Pa): After a patient has been assisted with a circulatory support device, either the patient's heart recovers and can be weaned from the device or the patient can be considered for cardiac transplantation. At Allegheny General Hospital an FDA approved and commercially available blood pump (Bio-Pump, Bio-Medicus, Eden Prairie, Minn) has been used experimentally and clinically to support failing ventricles (Fig 1). Based on our earlier experience, once the postcardiotomy patient is on ventricular assist, a minimum of 24 hours should be allowed before attempting to wean the patient from the device. Catastrophic results usually happen after weaning prematurely, even though the heart seems to be doing well at an early time.

Continuous monitoring during ventricular assist is absolutely necessary. A Swan–Ganz catheter, in addition to the arterial and venous pressure lines, is normally inserted. Most of our patients who receive ventricular assist also are supported by an intraaortic balloon pump. Once the patient has been on the ventricular assist device for more than a day and has been stabilized with a good indication of improvement in cardiac function, weaning can be considered. During biventricular assist, the ventricles may regain their function at different times, and the removal of one pump several days before the other is possible. However, weaning from both pumps at the same time is easier to manage and to the patient's advantage.

Patient J.O. will be used as an example of weaning from circulatory support. As shown by Fig 2A, the pump was running at 4 L/min and the balloon at 1:1, pulmonary arterial (PA) pressure was 29/12 mm Hg and cardiac output (CO) was 4.57 L/min. During ventricular assist a minimal flow of 4 L/min or a cardiac index above 2 L/min/m^2 is recommended. When the balloon was put on 1:2 with a pump flow of 4 L/min (Fig 2B), no ventricular pressure was generated, and the patient was obviously not ready to be weaned from the support. Twelve hours later, when the pump flow was temporarily decreased to 2.5 L/min with the balloon at 1:1 (Fig 2C), CO was maintained at 3.7 L/min, but a high PA pressure (51/27 mm Hg) was found. This indicated that his left ventricle was still not functioning normally.

Later (Fig 2D), when the pump flow was decreased to 2 L/min with the balloon off, the CO was 3.8 L/min. Even though the heart was generating 1.8 L/min of flow, the high PA pressure (55/29 mm Hg) was a contraindication for weaning. Prostaglandin E or any pulmonary vessel dilator is useful for decreasing pulmonary vascular resistance. When the pump speed was decreased again to 3 L/min (Fig 2E) with the balloon at 1:1, good CO (4.1 L/min) and blood pressure and lowered PA pressure (44 versus 55 mm Hg) were observed. By further decreasing the pump and balloon assist (Fig 2F), blood pressure and CO were well maintained. The significant benefit from the intraaortic balloon could be easily seen at this time. When a patient is supported by the assist device, the activated clotting time is usually controlled at 170 seconds with heparin. When the pump rate is decreased below 2 L/min, the heparin dosage should be increased to minimize the potential of fibrin deposition. The centrifugal pump is impractical to operate at a flow rate much less than 0.5 L/min and should not be maintained at this rate longer than two or three minutes.

As cardiac function improves, ventricular assist devices can be turned off with the balloon on at 1:1 (Fig 2G). One should not turn the Bio-Pump off and leave the cannulas in place for a long time even with an increased dosage of heparin. We do not leave the cannulas in for more than five to seven minutes at any time. When the balloon is finally removed (Fig 2H), normal management can be

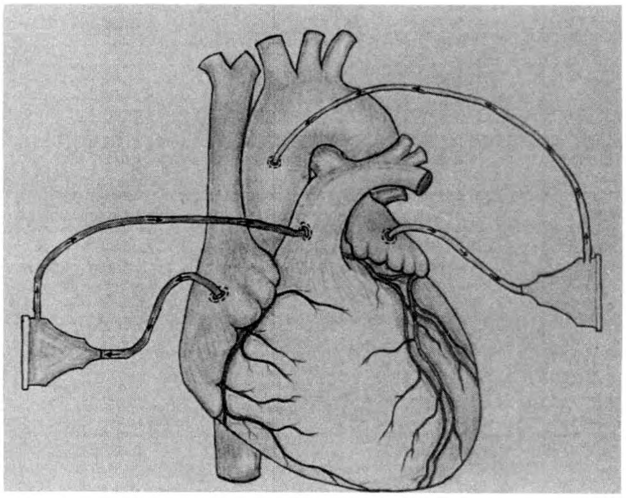

Fig 1. Biventricular assist. The left heart is supported by cannulating the left atrium and aorta. The right heart is assisted by cannulating the right atrium and pulmonary artery.

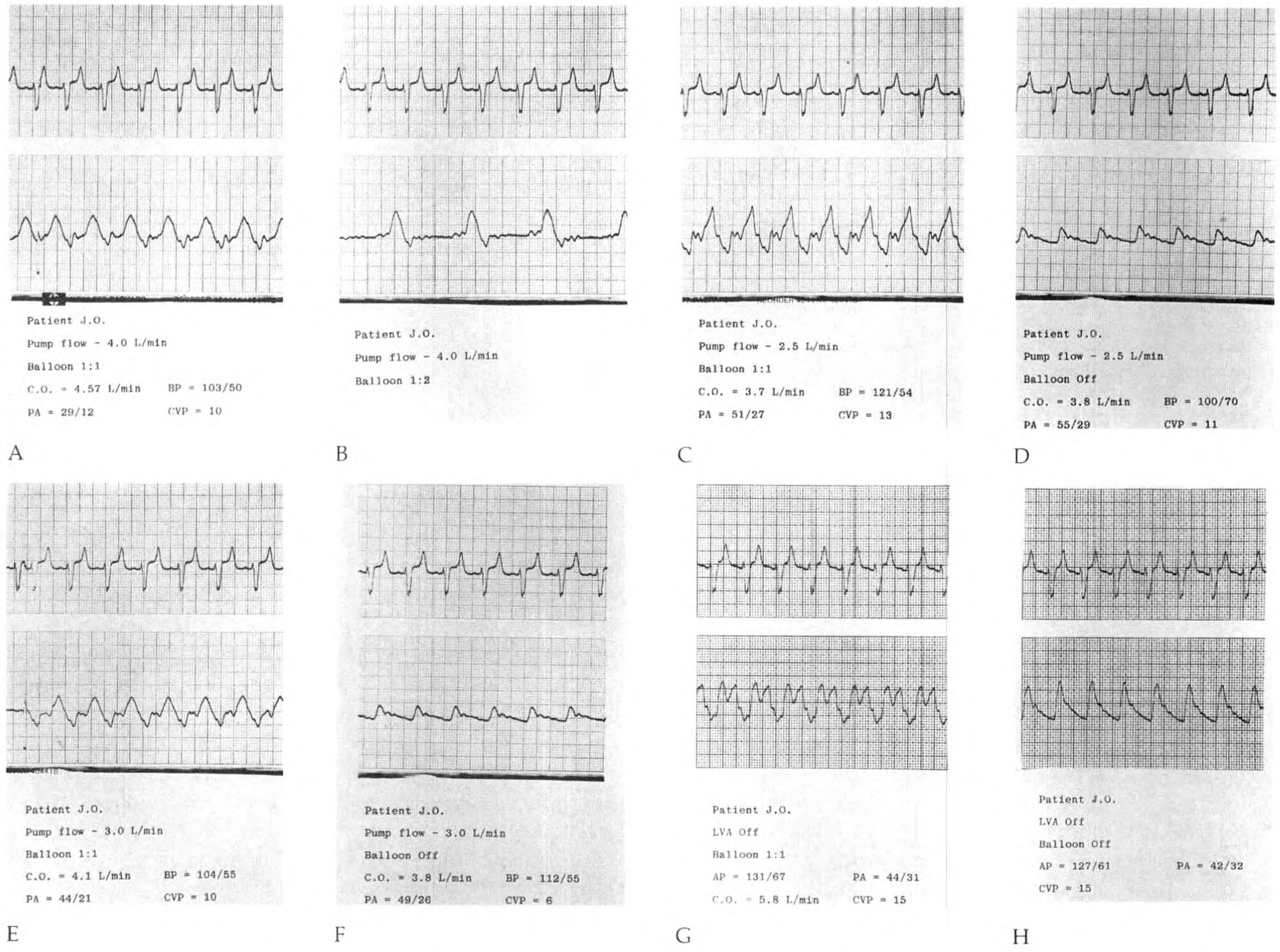

Fig 2. Hemodynamic parameters during ventricular assist and weaning. The ventricular function can be estimated by temporary reduction of the balloon pump and Bio-Pump support. Continual monitoring of cardiac output (C.O.) and pressures provides guiding directions during weaning. (BP = arterial blood pressure; CVP = central venous pressure; PA = pulmonary arterial pressure.)

applied. If the pressures are followed by a gradual return of CO and electrocardiogram, the weaning can be easily achieved. Weaning for patients with just the right or left heart assist can follow a similar procedure. Early insertion of the assist device can prevent the heart from deteriorating to an irreversible point. In our experience, no survival has been achieved in patients whom we have attempted to take off the heart-lung machine four or more times before ventricular assistance. There is quite a difference between weaning after cardiotomy and maintaining someone as a bridge to transplantation. The device will perform much better for patients who have not undergone several hours of bypass.

At Allegheny General Hospital during the period from July 1980 to December 1987, a total of 8,979 open heart operations were performed. Only 60 (0.67%) of these patients required ventricular assist. As shown by Table 2, 53% of this small group of moribund patients were weaned from the assist device. With improvement in management and advancement in experience, a long-term survival rate of 44% has been achieved by our recent group of patients supported by the Bio-Pump. One pa-

Table 2. Results in Patients Receiving the Bio-Pump as a Ventricular Assist Device

	Long-Term Survivors				Short-Term Survivors				Nonsurvivors			
Years	LVA	RVA	BVA	Total	LVA	RVA	BVA	Total	LVA	RVA	BVA	Total
1980–1984	6/25	1/2	0/1	7/28 (25%)	5/25	0/2	0/1	5/28 (18%)	14/25	1/2	1/1	16/28 (57%)
1985–1987	5/12	0/1	9/19	14/32 (44%)	4/12	0/1	2/19	6/32 (19%)	3/12	1/1	8/19	12/32 (38%)
1980–1987	11/37	1/3	9/20	21/60 (35%)	9/37	0/3	2/20	11/60 (18%)	17/37	2/3	9/20	28/60 (47%)

BVA = biventricular assist; LVA = left ventricular assist; RVA = right ventricular assist.

Table 3. Bridge to Transplantation at Allegheny General Hospital

Patient	Age (yr)	Type of Assist	Status	Hours on Assist
J.B.	39	Biventricular	LT	44
R.W.	45	Biventricular	ST	332.5

LT = long-term survivor; ST = short-term survivor.

tient, 12 months after being weaned from the ventricular assist device, has undergone cardiac transplantation.

As indicated by Table 3, we have used the Bio-Pump as a bridge to transplantation in 2 patients. The first patient was transferred to the University of Pittsburgh for cardiac transplantation while he was on biventricular assist from Allegheny General Hospital before we had our transplantation program. The patient is doing well with an uneventful recovery. The second patient is a man who developed cardiogenic shock due to massive myocardial infarction without previous operation. After being on biventricular assist for 2 weeks while waiting for a suitable donor heart, he was weaned from the device and removed from the transplant list. Although he never received a transplant, the Bio-Pump was essentially used as a bridge to transplantation.

The ventricular assist device decreases the workload of the failing heart and increases the blood flow through the coronary system and the vital organs. When the Bio-Pump was used for patients who could not be separated from cardiopulmonary bypass after open heart operation, 63% of the patients were weaned from circulatory support, with 44% of them as long-term survivors (from 32 patients during 1985 to 1987). Patients who suffer from cardiogenic shock due to acute myocardial infarction can be stabilized with circulatory assist for medical and surgical treatment. In addition, mechanical circulatory assist devices can be used as a bridge for patients awaiting cardiac transplantation.

DR P. E. OYER (Stanford, Calif): Our experience has been virtually limited to the use of the Novacor left ventricular assist device as a bridge to transplantation. This is an electrically powered device with wire coming through the skin, rather than a pneumatic tube or a blood containing tube. This makes infection less likely to happen with the Novacor device.

The Novacor device has been used to assist cardiac function with the native heart in place. The outflow vascular conduit consists of a 22-mm Meadox Cooley Veri-Soft woven Dacron graft that is commonly anastomosed to the aorta. However, on one occasion the supraceliac aorta was used as the return site. The pump inflow graft from the left ventricular apex to the pump has been used in all of our cases. The inflow conduit consists of a Hancock apical connector attached to a Dacron-covered polypropylene apical cannula. This system allows virtually complete decompression of the left ventricle. Left ventricular pressure measured in the patients during the assist period has never exceeded 40 mm Hg. Most of the time the pressure is 10 to 15 mm Hg within the left ventricle.

At Stanford we have had 7 patients use the Novacor for left ventricular assist, with 5 of them receiving heart transplantation. All of the patients had a cardiac index of well below 2 L/min with the exception of the first patient, whose problem really was coronary disease. He was waiting for transplantation, and he had intermittent bouts of angina, during which his cardiac index would indeed drop below 2 L/min. These episodes became gradually less controllable, and the device was implanted.

The preoperative PA systolic pressure has not been a concern to us in the selection of patients receiving an assist device. None of the patients at Stanford had a right ventricular device, even patients with high PA pressure. The success can be reflected by the fact that this device with apical cannulation may better unload the left side of the heart and reduce left atrial pressure to a range of 0 to 5 or 6 mm Hg. This is an important contribution in reducing the right ventricular afterload, which can cause high PA pressure. With selective pulmonary vasodilating agents, particularly prostaglandin E_1, the right-sided failure can be managed without a right ventricular assist device. This is supported by the high cardiac outputs seen in our patients at later times with only left ventricular assist. The cardiac output is always above 5.5 L/min and very frequently runs from 7.5 to 8 L/min.

Of our 7 patients, 5 underwent transplantation and 2 were not transplanted due to contraindications that developed during ventricular assistance. These 2 cases reflected several important issues for management and selection of bridging patients. One patient, our second patient, had a cardiac arrest the night before ventricular assistance, very poor liver function, elevated enzymes, and very high pulmonary resistance. This high pulmonary resistance also resulted in a low cardiac output immediately after the implantation of the device. Selective pulmonary vasodilating agents, particularly prostaglandin E_1, were used to correct the resistance. Cardiac output of 7 to 8 L/min was established once the high resistance and right-sided failure were corrected. In a couple of other patients prostaglandin E_1 was used prophylactically at the time of insertion of the device.

Another patient, who died in the operating room, was a patient who had a transplantation 3 months earlier. Her first transplant was hyperacutely rejected, and a centrifugal device was implanted into her transplanted heart immediately at the time of that transplantation for a period of 24 hours. She received a new transplant the next evening with a routine course of recovery. Three months later, when she had a severe acute rejection, the decision was made to implant the Novacor device.

In the case of severe ongoing uncontrollable rejection, the insertion of an assist device can be a fatal mistake. Manipulation of the rejected heart could further accentuate the already present edema. The ventricle is essentially at a stage of standstill due to the edema. Therefore, a cautious and discrete selection of patients is necessary for the use of ventricular assist devices as a bridge to transplantation.

The last patient was a young woman with postpartum cardiomyopathy and a wide open mitral regurgitation. The device functioned very well with a cardiac output of 5 to 7.5 L/min throughout the entire 35 days during which she was supported by the device. She was transplanted on Christmas Eve and went home about 21 days thereafter.

The Novacor device is an electrically powered, reliable device. No mechanical failure or embolic complications have occurred in our experience. Low doses of heparin have been used for most patients during ventricular assist. The last patient received no anticoagulation except low molecular weight dextran during the first week and oral aspirin and Persantine for the duration of her course. The pulmonary capillary wedge pressures, cardiac output, and other pressures are monitored during the support circulation. Several patients have also had an intraaortic balloon implanted. The controversial issues regarding improvement of patient management will be resolved as more data are available on bridging to transplantation.

DR C. CABROL (Paris, France): I wish to thank the organizing committee who invited me to such an outstanding meeting. We have used cardiac assistance devices in more than 20 cases, but I will present only the use of the Jarvik-7 total artificial heart as a bridge to transplantation.

From the very beginning, our policy has been to perform transplantation in only the patients in whom the artificial heart effectively restored a satisfactory and stable multiorgan condition. The hemodynamic status of the patients should be good before transplantation. Normal cardiac output with acceptable arterial and atrial pressures should be maintained under a moderate amount of drugs and minimal manipulation of the device parameters. The patients should have normal blood gases, satisfactory urine output with a negative fluid balance, and an improvement of hepatic function. The patients should not have important coagulation trouble, infection, fever, or elevated leukocyte count. Most importantly, we usually avoid putting these patients on the national priority emergency list.

Under these strict criteria, only 12 of the 30 patients in whom the Jarvik-7 was implanted were subjected to cardiac transplantation. In other words, only 40% of the patients supported by an artificial device received a donor heart. Three of the 12 patients who received transplants died, each from a different cause. One died of fulminant hepatitis 1 week after the procedure. Another died because of irreversible acute rejection 2 weeks after transplantation. The third patient had postoperative mental disturbances that incited him to disconnect the chest tubes, with a resulting massive pneumothorax and cardiac arrest. Resuscitation was too late to avoid brain lesions, of which he died 1 month later.

During a follow-up of from 3 to 17 months, 75% (9 of 12) of the patients who received transplants were alive. However, 1 patient has a Kaposi sarcoma with negative serology that may be due to azathioprine treatment. Of the 9 surviving patients, 3 sustained severe acute rejection, 2 had infection, and 4 were free of any complications. In our series, the midterm outcome of bridging to transplantation appears to be similar to conventional orthotopic heart transplantation.

For the patients who were bridged to transplantation, the survival rate is better in the young patients (less than 40 years old, 80%) than the older ones. The patients with acute cardiac decompensation also have a better survival rate (75%) than the ones with long-lasting cardiac failure. No difference in etiology has been found between the patients with acute or chronic cardiac decompensation except for a peculiar group of patients who had the Jarvik implantation for a refractory rejection episode that led to death in spite of massive and multiple immunosuppressive therapies. All 4 of these patients died of sepsis caused by their massive immunosuppression, which provided a most favorable ground for infection.

In conclusion, our policy is to perform transplantation in patients with a Jarvik heart only when they are in about the same condition as an ordinary elective transplantation candidate. They should not have any temporary contraindications such as fever, coagulation trouble, pulmonary problems, or HLA antibodies. We prefer a young patient recovering from an acute cardiac decompensation with satisfactory and stable organ function (especially liver and kidney) and without heavy immunosuppression. When these conditions exist, the transplantation is scheduled without emergency, and the patient waits for a good donor heart. This policy explains why only 40% of the patients in whom the Jarvik-7 is implanted receive transplants, and also contributes to the 75% survival rate of patients bridged to transplantation. This survival rate is about the same as for our 450 conventionally transplanted patients. Our policy avoids the bitter failures commonly observed after bridging to transplantation and the wasting of good donor hearts, which are so desperately needed by the 200 elective candidates waiting on the transplant list.

Discussion

DR MAGOVERN: Dr. Cabrol's point is well taken. One should not rush into transplantation for patients on ventricular assistance. Most of the mechanical devices are quite reliable and hematological parameters can be easily managed. Dr Golding, do you agree to this?

DR GOLDING: Yes, I agree. From our early experience, rushing into transplantation is not recommended, particularly if the patient's course was complicated by infection during circulatory support. The patient's condition can be optimized into that of an elective candidate by treating the sepsis, allowing the wounds to heal, and strengthening the patient with nutritional management.

DR OYER: I certainly agree. Several donors were available but were not used for the patients being bridged at our institution because the patients were not fully recovered enough to have the strength for the transplantation procedure. It is better to wait and allow the patient to be stabilized before the weaning or bridging.

DR GALBRAITH (Columbus, Ohio): I have a comment for Dr Oyer and a question for the panel. One of our patients at Ohio State University had acute failure of the transplanted allograft 5 months after orthotopic cardiac transplantation. During insertion of the circulatory assist device in the operating room, the rejection of both ventricles was evident, as proved by subsequent pathological examination. With biventricular assistance the patient was successfully bridged to transplantation. Therefore, patients suffering acute failure due to rejection of an orthotopic transplanted allograft should have biventricular support instead of just left heart assist.

The question is in regard to the use of standard immunologic screening mechanisms after bridging to transplantation. The percentage of reactive antibodies (PRA) is commonly used as a predictor of hyperacute rejection and rejection in patients who have received transplants. Is it necessary to use PRA in the patient who has been bridged to transplantation and has had essentially exchange transfusions with multiple blood transfusions and clotting factors? If it is necessary, when should we look at PRA, what levels should we use as an indicator, and when should we perform HLA crossmatching?

DR MAGOVERN: For biventricular failure, circulatory assist to both ventricles will be necessary. From our recent experience, the higher long-term survival rate can be attributed to the use of biventricular assist. In cases other than clear single ventricular failure, initiation of biventricular support will simplify patient management and avoid an extra operation to insert the second assist device.

DR OYER: It is correct that you may completely exchange-transfuse the patient at the time of transplantation after bridging. However, it may not be long before the reformation of antibodies that are truly reactive against the particular donor. A high level of PRA can also be caused by medication, especially some of the antiarrhythmic drugs. When a high level of PRA is observed, the drug effect must be ruled out first. Another way is to split, by looking at warm and cold T-cell crossmatches. If the high level of PRA is due to benign antigen antibody reactions, looking at specific cross-matches will improve the result.

This is a complicated problem. Through better sharing of information across the new donor procurement boundaries and giving high priority to the patients who are hard to cross-match, some of the difficulties may be alleviated.

DR CABROL: We are taking the same precautions. Fortunately we only have 1 patient who is sensitized and waiting for a negative cross-match. Long-distance procurement and retrospective cross-match are being done for the patient. Once a patient is sensitized you definitely have a big problem on hand.

DR JOHN MANNION (Philadelphia, Pa): Dr Golding is to be congratulated for the interesting and impressive results using the Bio-Medicus pump as a bridge to transplantation. Do you employ special procedures for cannula insertion, sternum closure, and extubation of patients? Having a patient supported by the Bio-Pump for 31 days before transplantation is a truly remarkable achievement.

DR GOLDING: Thank you. Cannulas varied a little but are mostly 32F or 36F venous cannulas. Ventricular drainage is necessary to avoid clotting and stroke. When atrium draining is used, a relative stasis is created in the ventricle. The cannula has to be positioned in the ventricle either through the apex or through the mitral valve when inserted into the left atrium or pulmonary vein. Ventricular drainage with the proper size of cannula is the way to success. Any practical way can be used for the arterial return. Three of the patients have been maintained on the device while they were depulsed, awake, and extubated.

DR GOMEZ (Peoria, Ill): For the patient with an intraaortic balloon who is supported by a centrifugal pump, weaning to the balloon and mild inotropic support seems the approach. What are the criteria to wean the patient who is supported by a pulsatile device to the balloon and mild inotropic support or to the patient's own heart to sustain circulation?

DR WILLIAM S. PIERCE (Hershey, Pa): We have weaned a modest number of patients from the pneumatic ventricular assist device. We feel very strongly that the balloon ought to be removed and that one should never plan to put it back once the assist device is in and functioning. Small doses of dopamine can be used for the renal effect but not for the cardiotonic effect. We want to wean the patient so that he or she will be independent of drugs and the balloon pump. A reliable circulatory support system that can function long enough to allow good myocardial recovery is the secret of success.

Circulatory Support With a Centrifugal Pump as a Bridge to Cardiac Transplantation

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Since January 1985, the Heart Transplant Program at Washington University Medical Center, St. Louis, has performed 89 heart transplantations in 86 patients. Twenty patients (23%) have required preoperative mechanical support of circulation or respiration prior to transplantation. The Bio-Medicus centrifugal pump (Bio-Pump) formed the basis of our circulatory support system during the period of this report. Nine patients were placed on the Bio-Pump with the intention of bridging them to transplantation. Six patients required left ventricular assistance; in 2, the device was inserted because they could not be weaned from cardiopulmonary bypass. Two patients required biventricular assistance, 1 because she could not be weaned from cardiopulmonary bypass at the end of a cardiac operation. Extracorporeal membrane oxygenation was necessary in 1 patient for right ventricular decompensation and cardiac arrest four hours after orthotopic cardiac transplantation. One of these 9 patients died on circulatory support, and in another, a complication developed that precluded transplantation. The remaining 7 patients (78%) underwent a successful transplant procedure after an average of 1.6 days of circulatory support (range, 0.5 to three days), and all are long-term survivors of transplantation. There has been 1 late death at 17 months from a cerebrovascular hemorrhage. In summary, the centrifugal pump provides excellent short-term circulatory support for individuals who would otherwise die before cardiac transplantation.

(Ann Thorac Surg 1989;47:108–12)

Advances in the efficacy of cardiac transplantation have dovetailed with the availability of a plethora of biomechanical devices to allow the salvage of individuals who previously would have died. Stimulated by the advent of heart transplantation at Washington University in St. Louis, our group [1, 2] has had a large experience with circulatory support in attempting to salvage and maintain patients until a donor heart can be located. This report details our experience with the Bio-Medicus centrifugal pump (Bio-Pump; Bio-Medicus, Eden Prairie, Minn) in the support of such patients.

Material and Methods

Since January 1985, the Heart Transplant Program at Washington University School of Medicine, St. Louis, has performed 89 heart transplantations in 86 patients. Twenty of these individuals (23%) have required mechanical support of circulation or respiration. This report focuses on 9 individuals supported with the Bio-Pump for left ventricular or biventricular assistance or for extracorporeal membrane oxygenation (ECMO). The 9 patients ranged in age from 16 to 57 years with a mean of 42 years. The cardiac diagnoses are outlined in Table 1. Two thirds of the patients had ischemic heart disease. The condition of all patients had deteriorated to such a point that ventricular assistance or ECMO was required to sustain them until a donor heart became available (Table 2).

Device Insertion

The Bio-Console (model 520D) (Bio-Medicus) was used to provide circulatory support in the 9 patients. For left ventricular assistance, left atrial–aortic bypass was employed. A 36F right-angle cannula (Polystan A/S, Ballerup, Denmark) is inserted into the roof of the left atrium at its junction with the right superior pulmonary vein with the cannula tip directed to the middle of the left atrium as previously described [1]. Aortic cannulation is performed low in the ascending aorta with a standard aortic cannula. The cannulas are held in place with pursestring sutures and Rumel tourniquets.

For right ventricular assistance, the venous cannula is inserted into the right atrium through a pursestring suture placed inferiorly in the right atrium in such a way that the tip of the right-angle cannula can be directed through the tricuspid valve. A standard arterial cannula is placed in the pulmonary artery.

For biventricular assistance, cannulation is as described for left ventricular and right ventricular assistance in combination.

To institute ECMO, right atrial–aortic bypass is used with cannulation as already described.

In 7 patients in this series, the cannulas were brought out through the median sternotomy incision with the sternum left open and the skin closed. In 2 patients, the

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Table 1. Cardiac Diagnoses in Patients Supported as Bridge to Transplantation

Cardiac Diagnosis	No. of Patients[a]
Ischemic heart disease	6 (67)
Aortic insufficiency	1 (11)
Cardiomyopathy	1 (11)
Wolff–Parkinson–White syndrome with cardiomyopathy	1 (11)

[a] Numbers in parentheses are percentages.

chest could not be closed; a retractor was left in the sternum, and the cannulas were brought out in the midline. Heparin sodium is reversed in the operating theater with protamine sulfate to effect hemostasis. Once the patient is in the intensive care unit, and when mediastinal drainage is acceptably low, a continuous heparin infusion is instituted to achieve an activated clotting time between 150 and 200 seconds for individuals on left ventricular, right ventricular, or biventricular support, and between 250 and 400 seconds for individuals on ECMO. Patients are maintained on broad-spectrum antibacterial therapy during the period of circulatory support.

To assess adequacy of neurological function, all patients were allowed to awaken from anesthesia; several had sustained one or more cardiac arrests before the institution of circulatory support. Renal and hepatic function and infection status were also carefully surveyed. Attempts at weaning from circulatory support confirmed in each instance that the native heart showed no signs of recovery. Thus, all patients had to meet conventional criteria for transplantation before we could initiate a search for a donor organ.

Transplantation

At the time of orthotopic transplantation, attempts were made to remove the aortic cannulation sites with the diseased native heart to limit foci of infection. Orthotopic transplantation otherwise proceeded in routine fashion. Especially meticulous wound care was administered, including copious irrigation with antibiotic solution at the time of transplantation. Immunosuppression consisted of triple therapy with cyclosporine, azathioprine, and prednisone. Perioperative antibiotic prophylaxis consisted of vancomycin for 48 hours and cephalosporin until all invasive lines were removed. Specific infectious complications were treated according to the organism identified. All patients received Mycostatin (nystatin) orally and by nasal inhalation for the first 3 months, and were maintained on trimethoprim sulfamethoxazole prophylaxis indefinitely. Patients seronegative for cytomegalovirus before transplantation received exclusively cytomegalovirus-negative blood and blood products. All patients received cytomegalovirus hyperimmune globulin (R. Conti, University of Minnesota) 1 week and 1 month after transplantation.

Table 2. Summary of Data on Patients Given Circulatory Support with Bio-Medicus Bio-Pump

Patient No., Age (yr)	Cardiac Diagnosis	Circulatory Support (days)	CPB for Insertion	Flow Rate[a] (L/min)	Outcome
1. 46	Acute MI, cardiogenic shock	LVAD (3)	No	2.0–5.0 (3.5)	OHT; alive and well
2. 57	Perioperative MI during repeat CABG	LVAD (2)	Yes	1.0–2.5 (2.3)	OHT; alive and well
3. 48	Acute MI, cardiogenic shock	LVAD (0.5)	No	1.5–3.5 (2.0)	OHT; alive and well
4. 45	Failure to be weaned from CPB after third AVR	LVAD (1.5)	Yes	2.2–4.3 (4.0)	OHT; died at 17 mo
5. 45	Perioperative MI, cardiac arrest after CABG	LVAD (1)	Yes	2.0–4.0 (3.0)	OHT; alive and well
6. 32	RV failure, cardiac arrest after OHT	ECMO (1.5)	No	3.0–5.0 (4.0)	OHT; alive and well
7. 16	Failure to be weaned from CPB after WPW procedure	BVAD (4)	Yes	3.0–5.0 (4.0)	CVA on device
8. 44	Acute MI, cardiogenic shock	LVAD (1)	No	1.5–2.5 (2.0)	Died on device
9. 41	Perioperative MI, cardiac arrest after CABG	BVAD (1.5)	Yes	3.5–4.5 (4.0)	OHT; alive and well
Average 42		1.8 days		3.2	

[a] Data are given as a range with mean in parentheses.

AVR = aortic valve replacement; BVAD = biventricular assist device; CABG = coronary artery bypass grafting; CPB = cardiopulmonary bypass; CVA = cerebrovascular accident; ECMO = extracorporeal membrane oxygenator; LVAD = left ventricular assist device; MI = myocardial infarction; OHT = orthotopic heart transplantation; RV = right ventricular; WPW = Wolff–Parkinson–White.

Results

Left Ventricular Assistance

Six patients required left ventricular assistance. Three had experienced massive acute myocardial infarction and were in cardiogenic shock. One patient sustained a perioperative infarction during reoperative coronary artery bypass grafting and could not be weaned from bypass. Another patient could not be weaned from cardiopulmonary bypass after his third aortic valve replacement. One patient sustained a large perioperative myocardial infarction and cardiac arrest several hours after coronary artery bypass grafting.

In three instances, the Bio-Pump left ventricular assist device (LVAD) was inserted without the use of cardiopulmonary bypass. Each of these patients had sustained massive myocardial infarction and were in cardiogenic shock. The device was inserted utilizing a 36F right-angle cannula placed in the roof of the left atrium just posterior to the interatrial groove with routine aortic cannulation as previously described [1].

One patient, the first in our series, was a 44-year-old man who sustained a massive myocardial infarction and, when transferred to our hospital, was in cardiogenic shock and on an intraaortic balloon pump. The LVAD was placed, but because of substantial biventricular failure, it did not provide adequate support. The patient died before additional measures could be instituted. The other 5 patients supported with an LVAD were adequately resuscitated on the device and determined to be suitable candidates for cardiac transplantation. All 5 underwent a successful transplant procedure within 12 hours to three days, and are long-term survivors of transplantation. One individual died of an intracerebral hemorrhage 17 months after transplantation.

Biventricular Assistance

Two patients were supported with biventricular devices. One patient sustained a large perioperative myocardial infarction and cardiac arrest shortly after coronary artery bypass grafting. The patient was supported for 36 hours, and then a successful transplant procedure was performed. This patient is a long-term survivor of cardiac transplantation. The other patient was a 16-year-old girl undergoing surgical correction of Wolff–Parkinson–White syndrome who could not be weaned from cardiopulmonary bypass. She had an underlying cardiomyopathy in addition to Wolff–Parkinson–White syndrome, and was placed on biventricular support with Bio-Pumps. On the fourth postoperative day, she sustained a cerebrovascular accident and was declared brain dead. Thus, 1 of 2 patients supported with biventricular devices was deemed a suitable candidate for transplantation and underwent transplantation successfully.

Extracorporeal Membrane Oxygenation

One patient, a 32-year-old man, required support with an extracorporeal membrane oxygenator. He had undergone a routine orthotopic transplantation for cardiomyopathy several hours earlier. Acute right ventricular failure and cardiac arrest developed several hours after the transplant procedure. The patient was taken to the operating room with his chest open and internal massage being performed. Extracorporeal membrane oxygenation was instituted without the use of cardiopulmonary bypass. Thirty-six hours later, a second donor heart was located and transplantation was performed. The patient is a long-term survivor of transplantation, although he has mild neurological residua attributed to the prolonged cardiac arrest.

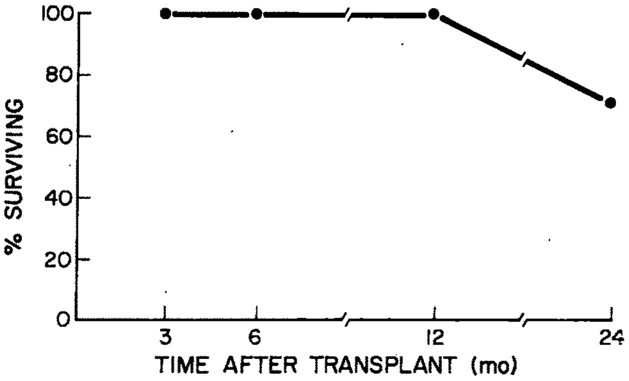

Fig 1. Survival of 7 patients supported with the Bio-Pump prior to transplantation.

Transplantation and Long-Term Outcome

Seven of these 9 desperately ill patients were deemed suitable candidates for cardiac transplantation while being maintained with various degrees of circulatory support. All 7 underwent a successful transplantation and were long-term survivors. One patient resumed use of alcohol postoperatively and was not able to be rehabilitated. He died 17 months after transplantation of alcohol-related pancreatitis and a cerebrovascular accident. The other 6 patients (86%) are alive and well, and have been rehabilitated to their premorbid level of activity. Actuarial survival in this group is 100% at 3, 6, and 12 months and 71% at 24 months (Fig 1).

Complications

Table 3 lists the complications that occurred in these patients supported with the Bio-Pump as a bridge to transplantation. There were seven events in 9 patients, a complication rate of 78%.

In 2 patients the complications proved fatal. One patient died of inadequate circulatory support. He was on an LVAD and died of biventricular failure before other measures could be instituted. He was the first patient in our circulatory support experience. In the other patient, massive cerebral edema, uncal herniation, and brain death occurred while she was on the device, and support was discontinued.

Two individuals sustained neurological damage as a result of cardiac arrest before the institution of circulatory support. *Enterobacter* septicemia developed in 1 patient after transplantation. Severe adult respiratory distress syndrome developed in another patient, who was given left ventricular assistance. Superficial wound dehiscence subsequently occurred in the same patient; it responded to conservative measures and healed without incident.

Table 3. Complications in Patients Supported as Bridge to Transplantation

Complication	No. of Patients[a]
Before transplantation	
Death on device	1 (11)
Cerebrovascular accident	
Before device insertion	2 (22)
After device insertion	1 (11)
After transplantation	
Sepsis	1 (11)
Adult respiratory distress syndrome	1 (11)
Superficial wound dehiscence	1 (11)
Total	7 (78)

[a] Numbers in parentheses are percentages.

The overall incidence of complications in this group is quite high. Fortunately, in the posttransplant setting, none of these complications proved fatal.

Rejection

Of the 7 patients bridged to transplantation, only 3 had any evidence of rejection during the first 3 months after transplantation. This is an incidence of 0.42 episodes per patient in the first 3 months, which is comparable to the incidence of rejection observed in our total patient experience [1, 2].

Comment

In appropriately selected individuals, heart transplantation has been demonstrated to be effective for increasing longevity and improving the quality of life. Many patients who are candidates for transplantation die while on the waiting list because of the current and ongoing shortage of available donors. In addition, some patients sustain severe myocardial damage as a result of a myocardial infarction or during attempted surgical repair of a cardiac lesion. Replacement of the heart becomes the only option for survival in these individuals. In the past, these patients would have died without the benefit of heart replacement—and many still do. In a few, however, as represented in this series, a catastrophic illness develops in a setting where facilities for mechanical bridging and heart transplantation are present.

The ventricular assist device has found increasing application in the support of patients with cardiogenic shock. Hill and associates [3] reported its use as a bridge to heart transplantation in a patient with postinfarction cardiogenic shock. The centrifugal pump enjoys widespread use in cardiac surgery and recently has been applied as a ventricular assist device for patients unable to be maintained in a conventional fashion. As reported previously, we [1] have devised a technique of cannulating the roof of the left atrium that provides satisfactory left atrial decompression when the device is used as an LVAD.

The centrifugal pump has been used in this series in a variety of circumstances. Two patients were in cardiogenic shock after massive myocardial infarction and could not be supported despite use of an intraaortic balloon pump and mechanical ventilation. Two other patients required the Bio-Pump in the operating room because they could not be weaned from cardiopulmonary bypass after cardiac surgical procedures. In 2 patients the pump was necessary for support following cardiac arrest in the wake of attempted coronary revascularization. The Bio-Pump, with the cannulation technique described, provides excellent short-term support of either the left or right ventricle. In addition, in 3 patients in our series, the LVAD was able to be inserted without the use of cardiopulmonary bypass. This obviates the bleeding problems attending full heparinization. We have found that maintaining the activated clotting time in the range of 150 to 200 seconds performs the dual purpose of preventing thrombus formation in the pump head and keeping the cannulas and cannulation sites free from thrombus and an associated cerebrovascular accident.

Extracorporeal membrane oxygenation was a lifesaving maneuver in the 1 patient in whom it was used in this series. The device was inserted following cardiac arrest several hours after a seemingly routine orthotopic transplantation. Right ventricular decompensation developed, rapidly eventuating in cardiac arrest and necessitating ECMO. Generally, ECMO is poorly tolerated in the adult population; we were fortunate to find a donor for this individual in the window of time available. Extracorporeal membrane oxygenation was instituted without the need for cardiopulmonary bypass in this patient, and this limited postoperative bleeding complications. Clearly, another option for this type of patient would be the total artificial heart [4].

Some interesting points have emerged from this small group of patients. The majority of patients requiring bridging had ischemic heart disease as the basis of their cardiac decompensation. As we [1] previously reported, after successful transplantation, patients bridged in this manner experience a slightly higher rate of infection in the first 3 postoperative months. The infections have been predominantly bacterial and may be related to the prolonged instrumentation attending the use of these devices. Mediastinitis did not develop in any patient in our series, regardless of whether bridging was required. This is gratifying and surprising in view of the multiple trips to the operating room that some of these patients required. The generally low rates of infection with the use of triple therapy in heart transplantation have been reported by our group [5]. Clearly, this played a role in the low rate of infection in these patients. In addition, there have been no fatal infections in this group of patients who required preoperative circulatory support. As mentioned, allograft rejection has occurred with approximately equal frequency in patients with and without bridging procedures.

The 2 deaths that took place during ventricular assistance were instructive. One patient, a 16-year-old girl, was on biventricular support for failure to be weaned from bypass after surgical correction of Wolff–Parkinson–White syndrome. Massive cerebral edema with brain stem herniation occurred. The generalized edema in patients on the Bio-Pump can be problematic, as in this young girl, and may be related to the absence of pulsatile flow. The other patient, a 44-year-old man with a massive myocardial infarction, died in cardiogenic shock despite an LVAD. Undoubtedly he had right ventricular failure as well, but died before additional support could be instituted. Many patients require support of both ventricles, as pointed out by Pennington and associates [6].

With the advent of pneumatic orthotopic devices, as well as extracorporeal devices and electrically driven implantable devices, one must raise the question as to the role of the centrifugal pump in circulatory support. As demonstrated by this small group of patients, short-term support is excellent with the centrifugal pump and bridging can be successful provided a donor is found in a short time. Clearly, donor availability is a critical limitation to transplantation in general and to the implementation of assist devices in particular.

Anecdotal reports of longer-term support (up to 31 days) with the Bio-Pump (Golding LR, Frazier OH; unpublished observations) encourage further development of the application of the Bio-Pump in bridging to transplantation. Golding and Frazier have utilized ventricular cannulation and have completely closed the sternum, thus making early mobilization of patients possible. This suggests that the Bio-Pump can provide longer-term support than has been appreciated. Nonetheless, in most hands the device has proved useful for only a few days at most. This limits the opportunity for the native heart to recover in the postcardiotomy setting and may force a premature decision as to transplant candidacy.

The pneumatic extracorporeal assist device (Thoratec Laboratories Corp, Berkeley, Calif) has yielded excellent results as a bridge to transplantation [7]. However, only 1 patient has been successfully bridged in the postcardiotomy setting. This suggests that the ideal candidate for bridging is the patient who is already on a transplant waiting list whose condition deteriorates before a donor heart can be found and who can be taken into the operating room and have a device implanted as a primary procedure. This individual has the best opportunity for long-term support if necessary, without the attending infectious complications.

The patient requiring ventricular assistance because of failure to be weaned from bypass at the time of a cardiac procedure is a less favorable candidate for a number of reasons. First, such patients are generally entirely unknown to the transplant service before a seemingly routine cardiac surgical procedure and therefore cannot be evaluated in a meaningful fashion. Second, devices inserted in the postcardiotomy setting of necessity are associated with a higher risk of both bleeding and infection than would otherwise be the case. This greatly compromises the chances of a successful transplant procedure in such an individual.

For these reasons, we believe the centrifugal pump should retain an important role in circulatory support. In patients on the transplant waiting list whose condition deteriorates prior to the availability of a donor heart, assist devices such as the pneumatic extracorporeal or the implantable electrically driven pumps are preferable in that they clearly provide safer long-term support. Recent isolated experiences suggest, however, that the Bio-Pump with certain modifications can also provide longer-term support. In the postcardiotomy setting, we must remain circumspect about individuals in whom any devices are inserted, as the overall results are quite dismal. Enough data have accumulated to allow us to take a realistic view of the unlikely possibility of successfully accomplishing transplantation in a patient in the postcardiotomy setting given the donor organ shortages. In this circumstance, we think that the centrifugal pump is the most logical choice for support because of its ease of insertion, reliability, general availability, and low cost. As our experience with this device increases, we will be able to support patients for longer periods.

In summary, in a small group of patients, the Bio-Pump centrifugal device provided excellent short-term support as a bridge to transplantation. This has been true in two settings: after a myocardial infarction and after cardiotomy. The device is readily available, inexpensive, and reliable. It is easy to insert and to monitor, and increasing experience will enhance confidence in its ability to extend the period of safe circulatory support.

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Surgical Techniques for the Implantation of Heterotopic Prosthetic Ventricles

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Mechanical support of the failing heart is becoming an increasingly useful tool for bridging to cardiac transplantation and for recovery of the natural heart. Several options exist for cannulation sites during the implantation of the heterotopic prosthetic ventricles. These options include the left atrial appendage, the left ventricular apex, the interatrial groove, and the left atrial roof. The indications, contraindications, advantages, disadvantages, and surgical technique for each option are described. Operation of the drive console and postoperative care are also discussed.

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Mechanical support of the failing circulation is becoming an increasingly important tool for the cardiac surgeon. Current indications for mechanical circulatory support are as a bridge to cardiac transplantation [1–4] and to allow recovery of the natural heart [5–7]. Candidates for implantation while their natural heart recovers are those with postcardiotomy cardiogenic shock, acute myocardial infarction with cardiogenic shock, or acute decompensation of the failing heart. The Pierce–Donachy prosthetic ventricle (Thoratec Medical, Inc, Berkeley, Calif), an experimental pulsatile pump placed in the paracorporeal position, is currently being evaluated in several centers worldwide. The combined results from centers in the United States, Japan, and Europe include the use of the ventricular assist device (VAD) in 129 patients [8]. The device has been implanted in 39 patients to bridge them to cardiac transplantation and in 90 patients to allow recovery of the natural heart. We describe the techniques for cannulation and implantation of the Pierce–Donachy prosthetic ventricle currently used in our institution.

Material and Methods

Pierce–Donachy prosthetic ventricles are pulsatile pneumatic blood pumps that can provide temporary circulatory support. The prosthetic ventricles are composed of a flexible, segmented polyurethane blood sac enclosed in a rigid polysulfone housing. A flexible polyurethane diaphragm divides the blood sac from the air inlet port. Unidirectional flow is maintained through the prosthetic ventricle by two Björk–Shiley mechanical valves located in the inlet and outlet ports. The device can be used for univentricular or biventricular support.

The Pierce–Donachy devices are placed in the heterotopic position lying on the anterior abdominal wall with the inflow and outflow cannulas passing transcutaneously and connecting to the heart and great vessels. The ventricles are driven by a pneumatic drive console, which can drive either one or two VADs. Separate sections of the console control each VAD independently.

The VADs will function in three modes. The asynchronous mode allows the device to pump at a set rate and a constant ejection fraction of 65 mL. The volume mode allows the prosthetic ventricle to eject each time the prosthetic ventricle is completely full; fullness is detected by a Hall switch located in the case of the prosthetic ventricle. A minimum rate can be set in the volume mode, although the filling may be incomplete with less than a 65-mL ejection. The external synchronous mode can be used to trigger the prosthetic ventricle from an external signal, the R wave of the electrocardiogram. The timing of the ejection can be set so that the prosthetic ventricle ejects after the ejection from the natural heart.

The other variable that can be controlled by the console is systolic percentage, the portion of time over which prosthetic ventricle ejection occurs. Varying the systolic percentage allows for a variation in the amount of time that the prosthetic ventricle has to fill.

A direct readout of VAD rate, systolic percentage, stroke volume, VAD output, ejection pressure, and fill pressure is present on the console. The amount of air pressure used to compress the blood sac of the prosthetic ventricle can be varied and is controlled from the console. Typically, the ejection force for left ventricular assist is 200 to 250 mm Hg and for right ventricular assist, 75 to 125 mm Hg. Vacuum can be placed on the blood sac of the prosthetic ventricle to increase the efficiency of filling and is controlled from the console. A fill vacuum of −25 to −50 mm Hg is sufficient for adequate VAD filling. Status lights for ejection, fill, and external synchronization as well as alarms for pressure, vacuum, synchronization, and low battery are present on the console.

For left ventricular support, inflow cannulation can be placed in the left atrial appendage, the left ventricular apex, the interatrial groove, or the left atrial roof. The

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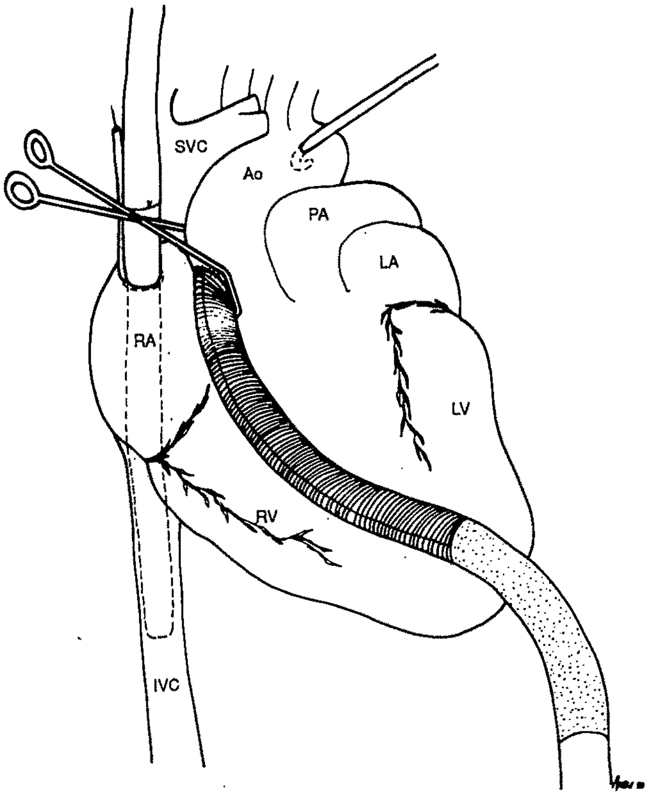

Fig 1. Placement of the outflow cannula for left ventricular support. Note the placement of the anastomosis on the greater curvature near the aortic root. (AO = *aorta;* IVC = *inferior vena cava;* LA = *left atrium;* LV = *left ventricle;* PA = *pulmonary artery;* RA = *right atrium;* RV = *right ventricle;* SVC = *superior vena cava.)*

atrial inflow cannula is a 51F right-angle venous return cannula coated with segmented polyurethane. The ventricular inflow cannula is a large-bore, wire-wound, segmented polyurethane tube fitted with a felt washer to permit suture fixation to the myocardium. For left ventricular support, outflow cannulation is to the ascending aorta, although the descending thoracic aorta has also been used for the outflow cannulation site. The outflow cannula is a large-bore, wire-wound, segmented polyurethane tube attached to a 14-mm Dacron graft. For right ventricular support, the inflow cannulation is in the right atrium and the outflow cannulation is to the main pulmonary artery. Both the inflow and outflow cannulas have felt collars positioned at the percutaneous exit sites of the cannulas. Accurate positioning of the percutaneous exit sites allows for tissue ingrowth, which in turn decreases the potential for ascending infection of the mediastinum.

Left Atrial Appendage

The most common method of implantation employs cardiopulmonary bypass with standard cannulation. Minimal dissection is necessary once cardiopulmonary bypass has begun because only separation of the aorta from the pulmonary artery is required.

The outflow cannula is prepared while cannulation for cardiopulmonary bypass and the dissection are proceeding. The Dacron graft is preclotted by soaking it in a 25% albumin solution and autoclaving the outflow cannula at 82.88°C for three minutes [9]. This markedly decreases the bleeding through the Dacron graft. If this step is omitted, there can be fatal hemorrhage from the graft because of the severe coagulopathies that can occur after the procedure. Simultaneously, the prosthetic ventricle is prepared by filling the ventricle with a 25% albumin solution to coat the blood sac; this enhances the removal of air from the system and lessens the incidence of thromboembolism.

The percutaneous exit sites for the cannulas are selected. For left ventricular support, the cannulas typically are brought out below the left costal margin. The cannulation incisions are through the skin and subcutaneous tissues with the fascial layers of the abdominal muscles incised in a cruciate fashion. The outflow cannula is measured to the appropriate length, and the Dacron graft is trimmed so that the felt collar of the cannula lies at the skin level as the cannula exits the mediastinum. The selection of the exit site for the atrial inflow cannula is crucial because the cannula is flared and, if shortened, will not connect properly to the prosthetic ventricle.

The outflow cannula is attached first to the ascending aorta. The outflow cannulation site for patients being considered for bridging to transplantation is along the greater curvature of the ascending aorta as low as possible near the aortic valve. This site allows for excision of the cannulation site at explantation of the prosthetic ventricle while leaving an adequate length of ascending aorta for the aortic anastomosis during transplantation. The cannulation site for the postcardiotomy group of patients is dictated by the presence of proximal vein graft anastomoses. A partial occluding clamp is placed on the ascending aorta, and a longitudinal aortotomy is made. The graft, which has been previously measured and beveled, is sewn in an end-to-side fashion using a running 4-0 polypropylene suture (Fig 1).

Atrial inflow cannulation is begun by placing a double pursestring suture of felt-pledgeted 2-0 polypropylene around the base of the left atrial appendage. The left atrial appendage is frequently too small for direct cannulation; in this case, it is necessary to extend the pursestring suture posteriorly onto the left atrial wall. The atrial septum is digitally explored through an incision in the left atrial appendage to detect a patent foramen ovale. If present, the patent foramen ovale must be closed before the insertion of the left atrial cannula to prevent right-to-left shunting. This is especially important in patients with only left ventricular support, as the right atrial pressure can exceed the left atrial pressure, particularly when vacuum is placed on the prosthetic ventricle. The right-angle atrial inflow cannula is placed through the atriotomy, and the suture is snared. The tourniquet is secured by tying the suture over a polypropylene button and to the outflow cannula (Fig 2). Both cannulas are passed through the percutaneous exit sites.

Removal of air is then necessary to prevent air emboli. A pursestring suture of 5-0 polypropylene is placed in the graft portion of the outflow cannula, and a vascular clamp is placed distal to that pursestring. A double-lumen Swan-Ganz catheter (American Edwards Laboratory, Irvine, Calif) is passed retrograde through the outflow cannula and placed across the outflow valve before the outflow cannula is connected to the prosthetic ventricle (Fig 3). The prosthetic ventricle, which has been filled with a heparinized 25% albumin solution, is attached to the atrial inflow cannula. The clamp on the inflow cannula is partially released to allow blood to escape while the outflow cannula is connected to the prosthetic ventricle. After the cannulas are secured, suction is placed on the Swan–Ganz catheter while the prosthetic ventricle is manipulated to allow for removal of residual air from within the prosthetic ventricle. The Swan–Ganz catheter and the clamp on the inflow cannula are removed.

After removal of all the visible air and with the vascular clamp still occluding the outflow cannula, pumping on the prosthetic ventricle is begun; blood is allowed to eject through the stab wound in the outflow cannula. This permits removal of any nonvisualized trapped air. No vacuum is placed on the ventricle while the chest is open because of the potential for introducing air into the left atrium and causing air emboli.

The vascular clamp is removed from the outflow cannula, and the exit site of the Swan–Ganz catheter is repaired. An accurate measurement of VAD preload is mandatory for optimum function. The pulmonary artery wedge pressure may not accurately reflect the left atrial pressure; therefore, a direct left atrial pressure line is placed through the right superior pulmonary vein. A micromanometer (Millar Instruments, Inc, Houston, Tex) is particularly useful, as it eliminates the potential for air emboli associated with fluid-filled catheters. Pumping is begun on the prosthetic ventricle, and separation from cardiopulmonary bypass is begun for patients not requiring biventricular support. Once the chest is closed, vacuum can be placed in the VAD to improve VAD filling.

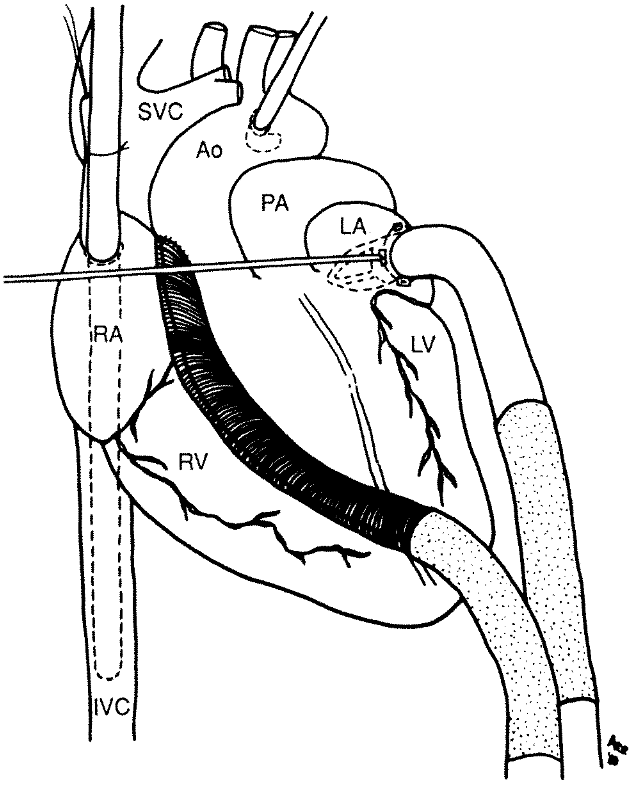

Fig 2. Placement of the left atrial inflow cannula for left ventricular support. Outflow cannula is in place. Abbreviations are the same as in Figure 1.

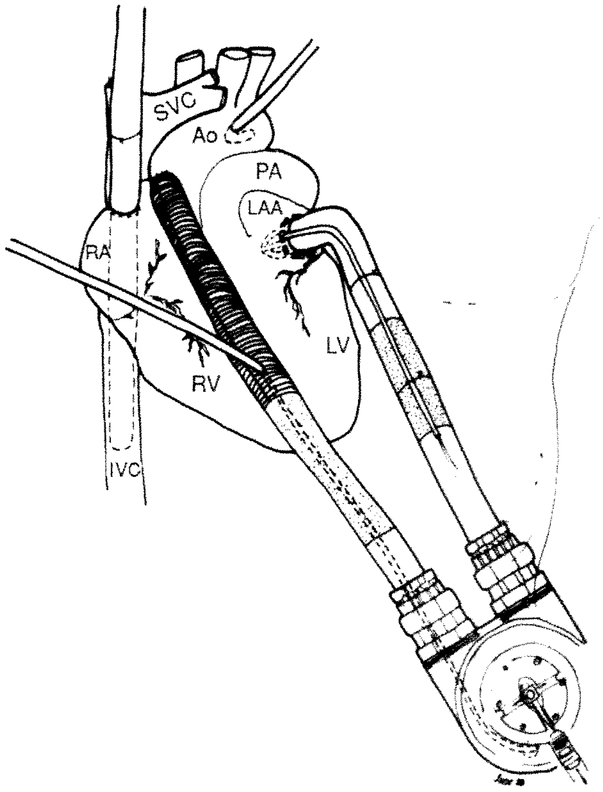

Fig 3. Completed cannulation with the prosthetic ventricle attached. A Swan–Ganz catheter is in place to remove air from the prosthetic ventricle. The clamp on the outflow cannula has been omitted for simplification. (LAA = left atrial appendage; all other abbreviations are the same as in Figure 1.)

Left Ventricular Apex

When the left ventricular apex is used for inflow cannulation, the initial conduct of the operation is the same as previously described. Additional dissection is necessary in the left subcostal region to allow for a direct exit of the inflow cannula beneath the costal margin. The pericardium is incised along the anterior diaphragmatic pericardial reflection, exposing the diaphragmatic attachments to the anterior chest wall and costal margin. These diaphragmatic attachments are bluntly dissected away from the anterior chest wall so that a space is developed allowing for a direct communication between the left ventricular apex and the left subcostal region. This permits proper orientation of the left ventricular apex cannula as it exits beneath the left costal margin. Proper selection of the percutaneous exit site is critical to allow the heart to lie in its normal anatomical position and to prevent kinking of the cannula. The percutaneous exit sites are determined and made.

A left ventricular vent is placed through the right superior pulmonary vein to decompress the ventricle and

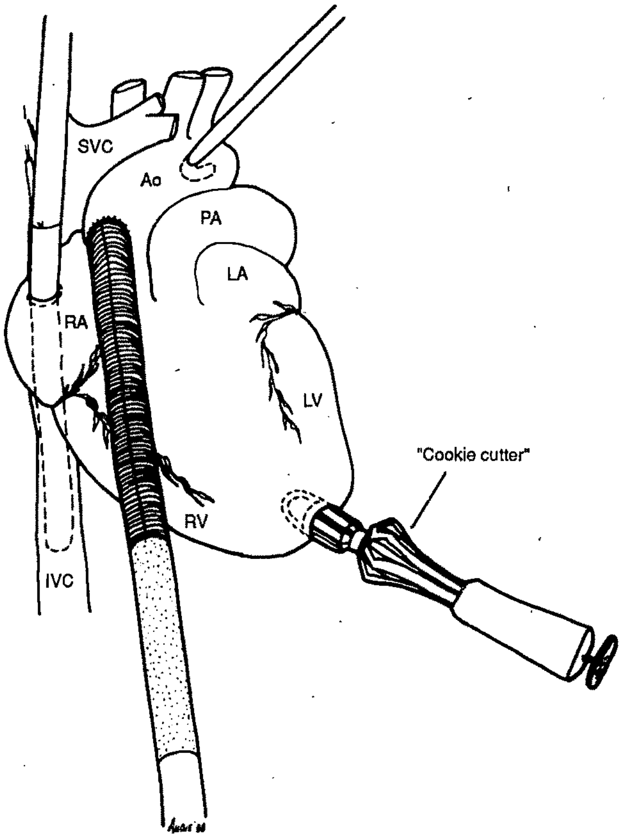

Fig 4. Preparation for placement of the ventricular inflow cannula using a Medtronic ventricular trocar ("cookie cutter"). Outflow cannula is in place. Abbreviations are the same as in Figure 1.

allow careful inspection of the left ventricular interior to visualize left ventricular mural thrombus. The outflow cannula is attached. A stab incision is placed in the left ventricular apex. A circular trocar (Medtronic Blood Systems, Anaheim, Calif) is used for the removal of a uniform circular portion of myocardium (Fig 4). The interior of the left ventricle is carefully inspected and any thrombus removed.

The inflow cannula is inserted, and circumferential felt-pledgeted 3-0 braided polyester sutures are placed to secure the felt washer of the inflow cannula to the myocardium (Fig 5). The inflow cannulation site must be absolutely hemostatic before the cannula is passed through the percutaneous exit site. Placement of additional sutures is nearly impossible once the cannula has been attached to the prosthetic ventricle, and fatal hemorrhage from the apex cannulation site can occur. Both cannulas are passed through the percutaneous exit sites, the prosthetic ventricle is attached, and the air is removed (Fig 6).

Right Ventricular Support

Right ventricular support is readily obtained for patients requiring either right ventricular support alone or biventricular support. In patients requiring biventricular support, the left ventricular prosthetic ventricle is placed first. Preparation of the right ventricular outflow cannula is similar to that used on the left. The exit sites for the cannulas are chosen in the right subcostal region, and no dissection of the pericardium is generally necessary.

The outflow cannula is placed first. A partial occluding clamp is applied to the main pulmonary artery. In the bridge-to-transplantation group, the position is critical and should be immediately distal to the pulmonary valve, thereby preserving the greatest length of pulmonary artery. An end-to-side anastomosis is performed using running 4-0 polypropylene suture. The inflow cannulation site of the right atrium is usually the right atrial free wall. Another possible cannulation site is the right atrial appendage; however, adequate inflow may not be achieved because of obstruction of the cannula when placed in this location.

The right ventricular inflow cannula can be placed while the patient is on cardiopulmonary bypass with the cardiopulmonary bypass cannulas in place. A felt-pledgeted 2-0 polypropylene pursestring suture is used for placement of the inflow cannula. A stab incision is made in the atrial wall and the right-angle inflow cannula

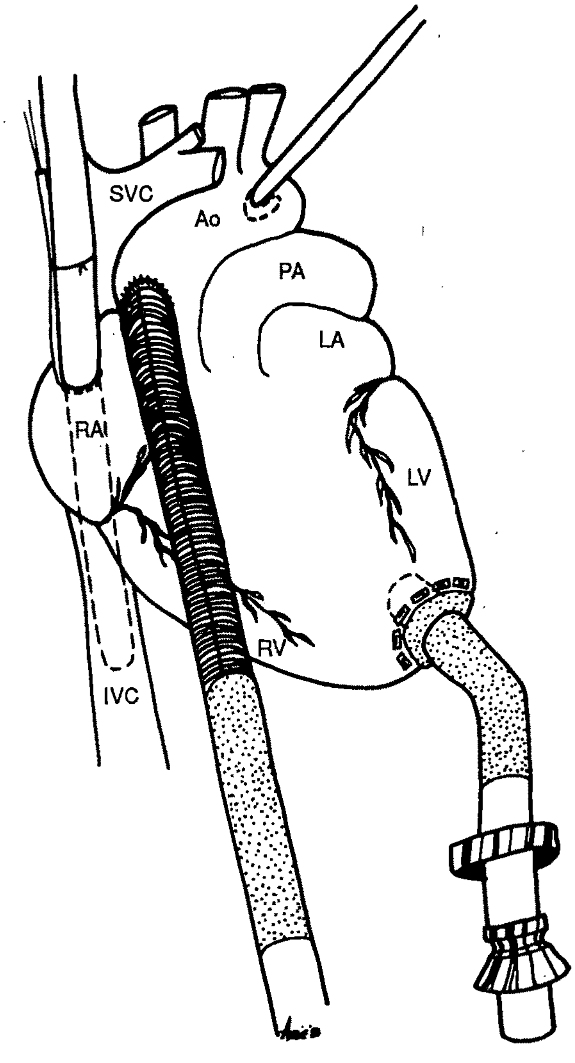

Fig 5. Cannulation for left ventricular support using the left ventricular inflow cannula.

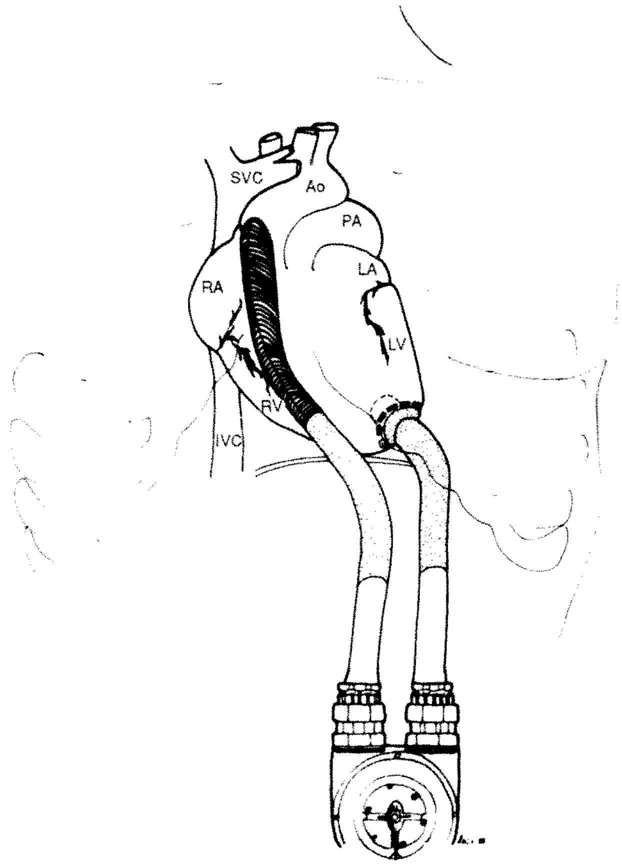

Fig 6. Left ventricular assist device in place showing typical percutaneous exit sites beneath the left costal margin. Abbreviations are the same as in Figure 1.

inserted. Both the inflow and outflow cannulas are passed through the percutaneous exit sites. To prevent crossing of the cannulas, the prosthetic ventricle is placed upside down with the inflow port on the right (Fig 7). Care must be exercised in connecting the cannulas to the appropriate ports on the prosthetic ventricle when oriented in this fashion.

Air is removed from the prosthetic ventricle. An accurate measurement of VAD preload is necessary for optimum function of the prosthetic ventricle, and the proximal port on a Swan–Ganz catheter is used to measure the central venous pressure. The Swan–Ganz catheter must be placed before the introduction of the inflow cannula. It cannot be readily positioned in the pulmonary artery after the cannula is placed and VAD pumping has begun because of the competitive reverse flow from the VAD toward the pulmonary valve in the proximal main pulmonary artery. Should it become necessary to remove and exchange the Swan–Ganz catheter in the postoperative period, the VAD must be turned off while the catheter is placed. A central venous line can be used; however, the cardiac output information obtained from the Swan–Ganz catheter can be important, as the natural heart can contribute a substantial amount to the total right-sided cardiac output. Pumping is begun on the prosthetic ventricles, and separation from cardiopulmonary bypass is possible.

Interatrial Groove

A third choice for inflow cannulation of the prosthetic left ventricle is through the interatrial groove along the right side of the heart. This is useful for patients not on cardiopulmonary bypass and is particularly useful in patients being bridged to cardiac transplantation.

The outflow cannula is prepared and placed as previously described. Placement of the inflow cannula in this location dictates that the precutaneous exit sites for the cannulas be placed in the right subcostal region, and is an important consideration before the percutaneous exit sites for the cannulas are made.

The interatrial groove is dissected, thus increasing the potential area for cannulation along the right side of the left atrium. A double pursestring suture of felt-pledgeted 2-0 polypropylene is placed and centered between the right superior and inferior pulmonary veins, thereby incorporating a portion of the opened interatrial groove to buttress the cannulation site. The cannula is not placed directly in the right superior pulmonary vein, as obstruction and thrombosis of the vein could occur. These maneuvers are readily accomplished without hemodynamic compromise, even in a patient whose condition is moderately unstable. Heparin sodium, 1 mg per kilogram

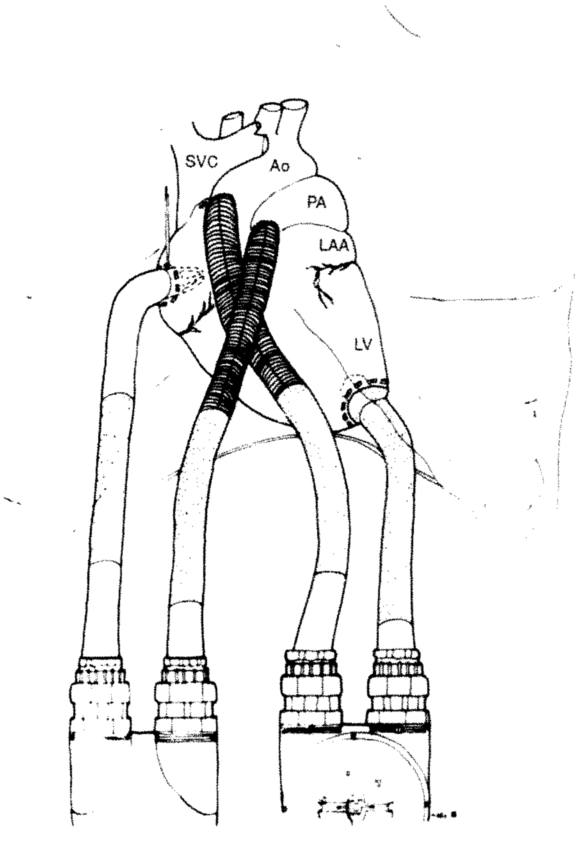

Fig 7. Biventricular support using left ventricular apex inflow cannulation. Note the orientation of the right ventricular prosthetic ventricle. (LAA = left atrial appendage; all other abbreviations are the same as in Figure 1.)

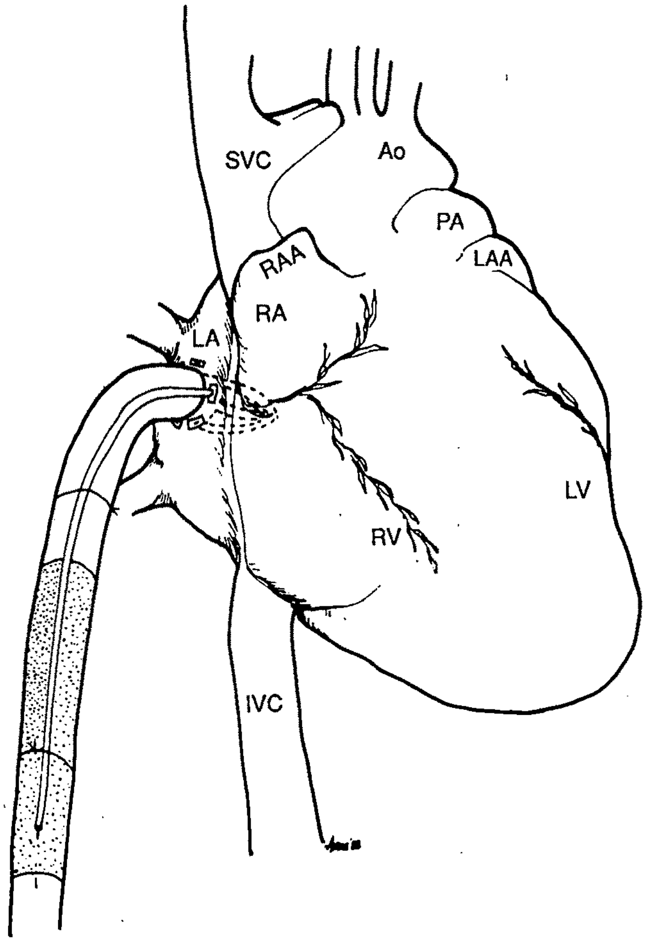

Fig 8. Location of the left atrial inflow cannula with the interatrial groove approach. Note the location of the insertion site between the pulmonary veins. The outflow cannula has been omitted for simplification. (LAA = left atrial appendage; RAA = right atrial appendage; all other abbreviations are the same as in Figure 1.)

of body weight, is administered. A stab incision is placed in the middle of the pursestring, and the inflow cannula is placed (Fig 8). The cannulas are then passed through the exit sites and attached to the prosthetic ventricle. The prosthetic ventricle is oriented with the inflow port on the right (Fig 9). Air is removed from the ventricle and ventricular support is begun.

For patients requiring biventricular support, the initiation of left ventricular support generally achieves hemodynamic stabilization so that cardiopulmonary bypass is not necessary. Right ventricular cannulation is similar to that previously described except the exit sites for the right prosthetic ventricle must be in the left subcostal region. The prosthetic ventricle is oriented upside down with the inflow port on the right, which allows a direct route between the heart and the prosthetic ventricle without crossing of the cannulas. Biventricular support is begun after the cannulas are attached and the air is removed from the prosthetic ventricle.

Left Atrial Roof

A fourth potential location for left ventricular inflow cannulation is the left atrial roof. This is achieved by retracting the ascending aorta to the left and the superior vena cava to the right. A double pursestring suture of felt-pledgeted 2-0 polypropylene is put in the left atrial roof, and the inflow cannula is placed. Outflow cannulation, connection of the cannulas, and removal of air from the prosthetic ventricle are as previously described.

Comment

The Pierce–Donachy prosthetic ventricle has proved to be a reliable and durable device as an aid to the failing heart. Although isolated right ventricular failure can occur, this is an infrequent event and most patients require placement of a left VAD as the initial step. The indications for left ventricular support include a cardiac index lower than 1.8 L/min/m^2, systolic arterial pressure lower than 90 mm

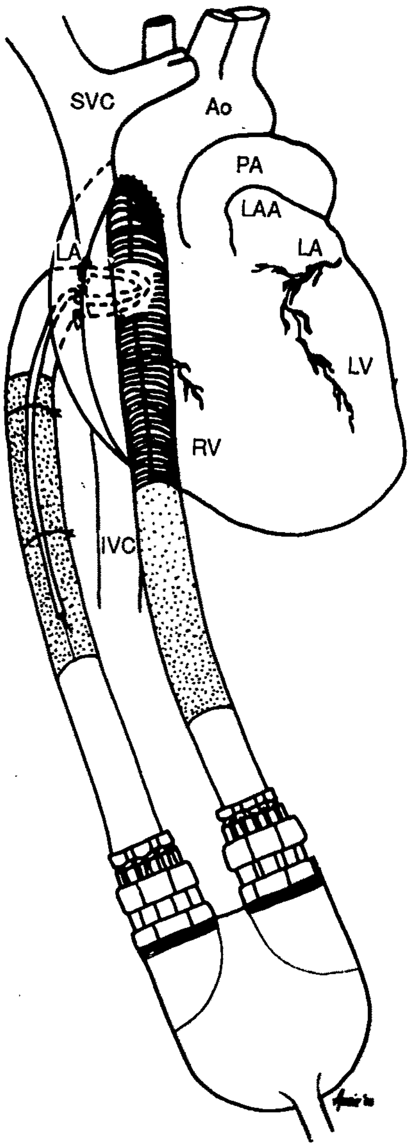

Fig 9. Completed cannulation for left ventricular support using the interatrial groove location for inflow cannulation. Note the orientation of the prosthetic ventricle. (LAA = left atrial appendage; all other abbreviations are the same as in Figure 1.)

Hg, left atrial pressure higher than 20 mm Hg in spite of pharmacological support, use of an intraaortic balloon pump, and correction of metabolic abnormalities.

The indications for placing a right VAD are less well defined. This decision is usually made in the operating room as separation from cardiopulmonary bypass is attempted with a left ventricular device in place. Our indications for right ventricular support include poor filling of the left VAD, left atrial pressure of less than 15 mm Hg with a central venous pressure of more than 25 mm Hg, and cardiac output as measured by the thermodilution Swan-Ganz catheter of less than 2 L/min. Important information for determining whether to place a right VAD is derived from inspection of the heart. Placement of a right VAD will be necessary if the right ventricle is distended and hypocontractile despite inotropic aid and left ventricular support. All patients needing only left ventricular support require inotropic support of the right ventricle. Despite adequate VAD function, most patients with a left VAD or biventricular assist devices require vasoconstricting agents such as epinephrine and norepinephrine for 48 to 72 hours because of the vasodilatory phenomenon.

Four potential sites are present for left ventricular inflow cannulation. These include the left atrial appendage, left ventricular apex, interatrial groove, and left atrial roof. Each site has specific indications, contraindications, advantages, and disadvantages.

The left atrial appendage has been used for either bridging to transplantation or recovery of the natural heart. Contraindications for the use of this location include a small left atrial appendage, previous cardiac operation with contracture of the left atrial appendage with adhesions, and body size greater than 100 kg, as the current atrial inflow cannula is too short to reach beneath the costal margin in patients with large chests. The principal advantages of this location are that no functioning myocardium is destroyed and that it is a technically easy location for cannulation.

Disadvantages of this location include the requirement of cardiopulmonary bypass for implantation. The inflow cannula poses a potential threat to grafts to the circumflex coronary artery if the device is used in the postcardiotomy patient. The inflow cannula must therefore be positioned away from the grafts by tacking the cannula to the anterior chest wall. A further disadvantage is that compression of the heart can occur when sternal closure is attempted with the cannula lying in this location. The inability to close the sternum and the resultant sternal instability may hinder extubation of the patient.

The left ventricular apex is ideally suited for the patient being bridged to transplantation. We do not think that this site is currently indicated for recovery of the natural heart, as viable myocardium is destroyed. Contraindications to the use of the left ventricular apex include a recent myocardial infarction involving the apex, which makes suture fixation of the inflow cannula to the myocardium tenuous and could even result in fatal hemorrhage, and small left ventricular volume, which could lead to inadequate inflow because of cannula obstruction. The advantages of the left ventricular apex include excellent drainage, particularly in the heart with a dilated cardiomyopathy, secure fixation to the heart, and applicability in a large range of body sizes as a result of the short distance between the left ventricular apex and the left subcostal percutaneous exit site. We have used this location without difficulty in patients weighing from 60 to 90 kg. Sternal closure is uniformly possible with the inflow cannula in this location. Disadvantages include the requirement for cardiopulmonary bypass for implantation and removal, difficulty in closing the cannulation site in the recovered heart, destruction of viable myocardium during cannulation, and potential hemorrhage from the cannulation site if cannulation is not perfect. Also, poor inflow is possible in patients with small left ventricular cavities.

The interatrial groove location is indicated in the patient being bridged to transplantation or for recovery of the natural heart. The contraindication to its use is a small left atrial volume. The principal advantage of this location is that it does not require cardiopulmonary bypass for insertion or removal of the VAD. Postoperative bleeding is reduced because minimal heparinization is required during implantation. No myocardium is destroyed, and there is less potential for injury to grafts to the left coronary artery system. Sternal closure is generally possible, and extubation is a realistic goal. The potential disadvantage is that of possible injury to grafts to the right coronary artery in the postcardiotomy patient.

The left atrial roof is the least useful cannulation location, but it can be used as a bridge to cardiac transplantation or for recovery of the natural heart. It is contraindicated in patients with a small body size and a small left atrium, as the cannula can obstruct, resulting in poor inflow. The advantage to this location is that no viable myocardium is destroyed during implantation. The disadvantages include the requirement for cardiopulmonary bypass for implantation, a technically more demanding insertion, the possibility of potential injury to right coronary artery grafts, and possible poor inflow with small atrial volumes. In addition, sternal closure may not be possible because of compression of the heart.

Postoperatively, the patients do require anticoagulation because each prosthetic ventricle has two mechanical heart valves as well as large surfaces of prosthetic material in contact with blood. Anticoagulation is not begun until the bleeding in the immediate postoperative period is at an acceptable level. Once the decision has been reached to begin anticoagulation, the intravenous administration of heparin, 1 mg/kg, is initiated. The partial thromboplastin time is monitored and is kept one and a half times normal. Anticoagulation therapy with low molecular weight dextran has also been used. Antiplatelet therapy with aspirin or dipyridamole may be appropriate in patients requiring long-term support. Cases of patients anticoagulated with Coumadin (crystalline warfarin sodium) have been reported.

Perioperative prophylactic antibiotics are administered as with any cardiac operation. Cefamandole nafate or cefazolin sodium are given intravenously, 1 g preoperatively every six hours for three days. The patients are maintained in reverse isolation. Surveillance cultures of the sputum, urine, and blood are grown. The potential for sepsis is great, and close monitoring for infection is necessary. Patients with positive cultures require prompt and vigorous treatment with appropriate antibiotics. The percutaneous exit sites of the cannulas are cared for by sterile dressing changes using an antiseptic solution such as dilute Betadine (povidone-iodine) or Dakin's solution three times a day. Local wound infections around the cannulation sites must be vigorously treated with surgical drainage and appropriate antibiotic therapy.

Operation of the console is straightforward and easy to master. The volume mode is useful in most situations, although the external synchronization mode has been advocated for recovery of the natural heart in a fashion similar to intraaortic balloon pump counterpulsation. It is not necessary to use the same mode or to maintain similar cardiac outputs between the two prosthetic ventricles in patients with biventricular support. The right VAD frequently is maintained with a smaller VAD output, as the right heart can contribute to the total right-sided cardiac output. The pulmonary vascular bed and the systemic vascular bed both have a great capacitance for storage of intravascular volume, and with improper setting of the VADs, pulmonary edema or anasarca can result. We have found the volume mode to be the most useful, and we use the asynchronous mode only in an effort to limit the output on the right VAD.

Monitoring of the preload from each VAD is necessary for optimal function in the volume mode. Inadequate intravascular volumes will result in poor filling of the prosthetic ventricles. Additional volume and increasing the vacuum on the prosthetic ventricle may improve VAD filling and increase VAD output.

The external synchronization mode may be useful for recovery of the natural heart and during weaning from the VAD. An appropriate delay can be programmed into the VAD so that the VAD ejection follows the natural heart ejection by a specified time.

Our experience with the Pierce–Donachy prosthetic ventricles began in March 1985, when biventricular support was used in a 16-year-old boy as a bridge to cardiac transplantation [1]. Biventricular support was utilized for six days. The patient is alive and well approximately 3 years after the transplantation. The Pierce–Donachy prosthetic ventricle has proved to be a reliable and satisfactory method for support of the failing heart. For placement of a left VAD, four potential inflow cannulations exist. Each of those cannulation sites offers its own distinct advantages and disadvantages. The implantation and programming of the device must be tailored to the specific needs of each patient.

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Percutaneous Cardiopulmonary Bypass: Application and Indication for Use

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Percutaneous cardiopulmonary bypass (CPB) was used in 22 patients: 7 patients with cardiac arrest due to acute myocardial infarction; 4 patients in cardiac arrest because of failed angioplasty; 1 patient for high-risk elective angioplasty; 1 patient with massive pulmonary emboli; 2 patients with hypothermia; 2 pediatric patients (1 with sepsis and 1 in combination with extracorporeal membrane oxygenator support); 1 patient with refractory arrhythmia; and 4 patients with trauma. Percutaneous CPB involves a modified Seldinger technique that is easily applied. All patients except those with massive trauma were resuscitated with the use of percutaneous CPB. One patient requiring a very difficult proposed angioplasty received percutaneous CPB support while triple-vessel angioplasty was performed. Percutaneous CPB appears to be beneficial in resuscitating patients with refractory cardiac arrest or other forms of circulatory collapse except trauma. Limited use for brief periods in high-risk patients having elective angioplasty might be applicable.

(Ann Thorac Surg 1989;47:121–3)

Emergency cardiopulmonary bypass (CPB) through surgical exposure of the femoral artery and veins is an accepted technique [1–4]. Although excellent cardiopulmonary resuscitation and support can be accomplished by this approach, it has never achieved widespread popularity for emergency application. Not only does it require a skillful surgical team, but it is difficult to implement in the environment where a patient is undergoing cardiopulmonary resuscitation. Traditional circulatory support systems such as intraaortic balloon pumping [5–11] have achieved popularity because of their effectiveness and ease of emergency application to patients in extremis.

The development of inexpensive large-bore, thin-walled percutaneously inserted sheaths [7] has allowed the extension of this technology for the development of a percutaneous cardiopulmonary support system utilizing standard equipment readily available from any cardiac surgical program [12]. This system can be rapidly applied by anyone familiar with percutaneous cannulation [13]. We have previously described our initial experience with this technique [12, 14, 15]. Percutaneous CPB has now been applied to 22 patients, and they are the subject of this expanded report.

Material and Methods

The details of the techniques for establishing percutaneous CPB have been described [12, 14, 16] and are briefly summarized here. Percutaneous cannulation of a femoral artery and both femoral veins is performed as follows: heparin sodium is administered, and the femoral artery and femoral veins are punctured. The skin over the puncture site is incised for 2 to 3 mm. A guidewire (Universal Medical Instruments Corp, Ballston Spa, NY) is introduced through the needle into the vessel followed by an introducer (dilator-sheath) assembly (Percor intraaortic balloon percutaneous introducer; Datascope Corp, Paramus, NJ). With completion of the cannulation of each vessel, the appropriate connections to the bypass tubing are made.

Arterial inflow is established through one femoral artery with an end-hole sheath. A large sheath (12F to 24F) is introduced into each femoral vein. Spaced side-holes can optionally be cut with a scalpel in the venous sheath to allow both end-hole and side-hole drainage. Perfusion is established with a portable pump and a pediatric oxygenator. The oxygenator is set as low as possible below the cannulation site to maximize gravity drainage. The arterial and venous tubing lengths are kept as short as possible to minimize resistance to flow. Appropriate resuscitative efforts are continued. Intermittent chest compression, if indicated, is applied to empty the heart and prevent distention.

The cases of all patients who underwent percutaneous CPB support were reviewed. Cause of arrest, length of resuscitative effort prior to percutaneous CPB, time to institute percutaneous CPB, time on percutaneous CPB, flow dynamics, and outcome were analyzed.

Results

Percutaneous CPB was used in 21 patients with refractory cardiac arrest and in 1 patient for hemodynamic support during high-risk angioplasty.

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The 21 patients in cardiac arrest were receiving good cardiopulmonary resuscitation. This included endotracheal intubation, chest compression, cardiotonic and antiarrhythmic drugs, intraaortic balloon pumping, and fluid administration. This group of patients with refractory cardiac arrest included the following: 7 with acute myocardial infarction, 4 with a failed angioplasty, 1 with pulmonary embolism, 1 with arrhythmia, 2 with hypothermia, 1 with sepsis, 1 in combination with extracorporeal membrane oxygenator support, and 4 with trauma. The 7 patients with acute myocardial infarction had refractory ventricular fibrillation for an average of 40 minutes prior to percutaneous bypass. In spite of all efforts to defibrillate them, they were unable to be returned to a regular heart rhythm until percutaneous CPB was instituted. All patients were successfully defibrillated after the initiation of percutaneous bypass. Percutaneous CPB was maintained for an average of 65 minutes. Three of these 7 patients survived and were discharged.

Of the 4 patients in whom angioplasty failed, 3 had refractory ventricular fibrillation and 1 was asystolic. Percutaneous bypass in this group averaged three hours. Three of the 4 patients underwent emergency coronary artery revascularization; there was 1 survivor. These 3 patients were resuscitated and transported to the operating room in a controlled fashion because their circulation was supported by percutaneous CPB. Routine preparation and draping were performed, and the patients were converted to conventional bypass through a standard sternotomy incision.

The fourth patient in whom angioplasty failed was resuscitated with percutaneous CPB. He did not have emergency coronary bypass grafting because he demonstrated a depressed neurological state. Immediate repeat angioplasty was performed, and all three major coronary arteries (right coronary, left anterior descending coronary, and circumflex coronary artery) were successfully reopened in the catheterization laboratory. The patient was then transported to the intensive care unit and was maintained on percutaneous CPB support for approximately eight hours. His condition became hemodynamically stable, and he was successfully weaned from percutaneous bypass. His neurological status normalized, and he was discharged from the hospital ten days after resuscitation. Before discharge, cardiac catheterization revealed all three coronary arteries to be patent with a left ventricular ejection fraction of 45%.

One patient required high-risk elective angioplasty. He was maintained on percutaneous CPB for approximately 15 minutes while high-risk triple-vessel angioplasty was carried out.

Two patients who were seen in the emergency room with hypothermia and refractory ventricular fibrillation were rewarmed by percutaneous CPB for approximately two hours. Both patients were successfully defibrillated, but 1 died secondary to multiorgan failure two days after percutaneous bypass.

One patient with a pulmonary embolus was asystolic. He was supported on percutaneous CPB for 40 minutes and then underwent emergency pulmonary embolectomy in a conventional fashion. The patient died two days after embolectomy.

One patient who had sudden refractory ventricular fibrillation six hours after aortic valve replacement was successfully resuscitated after three hours of percutaneous CPB. However, he died seven days later of complications of renal failure.

An 8-year-old patient was admitted to the hospital in septic shock secondary to mediastinitis. This patient was resuscitated after seven hours of percutaneous CPB but

Table 1. Summary of Patient Categories and Pertinent Data[a]

Cause of Arrest	No. of Patients	Rhythm	CPR Time (min)	Percutaneous CPB Time	Resuscitated	Alive
Acute myocardial infarction	7	Ventricular fibrillation	40	65 min	Yes	3
Failed PTCA	4	Ventricular fibrillation, 3; asystole, 1	20	3 h	Yes	2 (2 died postoperatively)
Elective PTCA	1	Sinus	None	15 min	. . .	1
Hypothermia	2	Ventricular fibrillation	30	2 h	Yes	1
Pulmonary embolism	1	Asystole	30	40 min	Yes	0
Sepsis	1	Bradycardia (asystole)	60	7 h	Yes	0
ECMO	1	Bradycardia (asystole)	. . .	36 h	Yes	2 days
Refractory fibrillation after AVR	1	Ventricular fibrillation	30	3 h	Yes	0 (died at 7 days)
Trauma	4	Asystole	30	60 min	3/4	0

[a] Flow rates averaged 2 to 3 L/min.

AVR = aortic valve replacement; CPB = cardiopulmonary bypass; CPR = cardiopulmonary resuscitation; ECMO = extracorporeal membrane oxygenator; PTCA = percutaneous transluminal coronary angioplasty.

died three days later of recurrent sepsis. A 4-year-old patient was maintained on a combination of percutaneous bypass and extracorporeal membrane oxygenator support for 36 hours, but also died two days after percutaneous CPB.

Resuscitation with percutaneous CPB was attempted in 4 patients with massive trauma. All 4 died of uncontrollable hemorrhage during the resuscitation attempt.

Cannulas larger than 12F in size required surgical removal. Cannulas 11F or smaller in size could be removed percutaneously with pressure applied to the cannulation sites. One of these latter patients required exploration of the femoral artery for thrombectomy. The patient categories are summarized in Table 1. Flow rates of 2 to 3 L/min were generally achieved.

Comment

Percutaneous CPB and other pump systems [1–3, 5, 12, 15–18] utilize external energy sources to support the failed circulation. The concept of percutaneous CPB is a melding of CPB technology with the technique for percutaneous vessel cannulation. The percutaneous CPB system "buys time." It is an easily applied technique for temporary circulatory support in a patient whose condition has not improved with conventional therapy. Percutaneous CPB was efficient enough to allow resuscitation in almost all of the patients (17/21); the 4 patients with trauma were the exceptions.

This simple, effective, and portable system provides a relatively safe mode for patient support and transport from the resuscitation site to the catheterization laboratory, operating room, or intensive care unit. Application of percutaneous CPB generally took fewer than five minutes. Our results indicate it was most effective for survival in patients whose arrest was related to cardiac causes. The results were poor in patients with trauma or septic shock. Although it is not a perfect system in terms of achievable flow rates and cannula sizes, the technique of percutaneous CPB can provide temporary lifesaving therapy until conventional bypass or definitive therapy can be instituted. Our limited experience suggests that some form of percutaneous CPB may be useful for elective high-risk percutaneous transluminal coronary angioplasty.

Although "total" support systems are being marketed (Bard, Billerica, Mass), their expense and complexity make them somewhat unattractive to us. Off-the-shelf equipment (eg, cannulas, tubing, pumps, oxygenator) can easily be combined to create an inexpensive and workable percutaneous CPB system. In addition, the creative cardiac surgeons and perfusionists have the latitude to improve the system described here with innovative modifications. This would not be possible with a commercially produced high-priced "fixed system."

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Technique and Results With a Roller Pump Left and Right Heart Assist Device

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During the last 10 years we have inserted a roller pump–driven left heart assist device in 72 patients and a right heart assist device in 7 patients for profound heart failure after a variety of cardiac surgical procedures. In addition a percutaneous left heart assist device (transseptal insertion of left atrial cannula via a femoral vein) was employed in 5 patients with profound cardiogenic shock after acute myocardial infarction. Thirty patients (41.7%) were weaned from the left heart assist device and 21 (29.2%) were discharged from the hospital. Two patients (40.0%) were weaned from the right heart assist device, but both later died during the postoperative period. Of the 5 patients in whom a percutaneous left heart assist device was inserted, 4 underwent successful emergency percutaneous transluminal coronary angioplasty, but all 5 patients died. Causes of death included severe coagulopathy, irreversible extensive myocardial infarction and cardiac failure, refractory arrhythmias, severe "shock" lung, and multisystem failure. In summary, satisfactory results can be achieved with a roller pump–driven left and right heart assist device for severe postoperative heart failure. Further experience should be obtained with the percutaneous technique to assess its efficacy in treating patients with acute myocardial infarction and cardiogenic shock.

(Ann Thorac Surg 1989;47:124–9)

Although profound heart failure following cardiac surgical procedures requiring the utilization of ventricular assist devices is relatively infrequent, there have been a number of reports of increasing success with the use of these devices [1–6]. Furthermore, the role of ventricular assist devices has expanded with their use as a bridge to transplantation [7, 8] and as a support device for patients with cardiogenic shock following myocardial infarction [9]. A variety of devices for ventricular assistance have been employed for this. We have used a roller pump–driven device since 1978, and this system is relatively effective, easy to use, and inexpensive. This report summarizes our experience with the use of a roller pump left heart assist device and right heart assist device, and also a newly developed percutaneously inserted left heart assist device.

Material and Methods

Since January 1978 at New York University Medical Center, New York; July 1982 at Maimonides Medical Center, Brooklyn; and January 1986 at the State University Hospital, Health Science Center at Brooklyn, we have utilized a left heart assist device in 72 patients and a right heart assist device in 7 patients after cardiac surgical procedures. In addition, a percutaneously inserted left heart assist device has been used in 5 patients with profound cardiogenic shock following acute myocardial infarction.

Indications for Use

LEFT HEART ASSIST DEVICE. Indications for use of a left heart assist device were either an inability to discontinue cardiopulmonary bypass (57 patients) or cardiac arrest one to 12 hours postoperatively (15 patients) (Table 1). About one fourth of the patients who could not initially be weaned from cardiopulmonary bypass (15/57) sustained cardiac arrest before bypass, either during cardiac catheterization, attempted percutaneous transluminal coronary angioplasty, or induction of anesthesia. Standard techniques were employed in attempting to discontinue cardiopulmonary bypass. They included volume loading, atrioventricular pacing, infusion of inotropic agents, and insertion of an intraaortic balloon. All patients demonstrated severe left heart failure with an elevated left atrial pressure (<25 mm Hg) and systemic hypotension (mean blood pressure <50 mm Hg), and cardiopulmonary bypass could not be discontinued without the use of a left heart assist device.

Fifteen patients sustained cardiac arrest postoperatively as a result of graft spasm (6 patients), refractory arrhythmias (6 patients), or acute graft thrombosis (3 patients). These patients required reinstitution of cardiopulmonary bypass to be resuscitated and insertion of a left heart assist device to be weaned from cardiopulmonary bypass.

RIGHT HEART ASSIST DEVICE. This group comprised 7 patients (see Table 1). Isolated right heart failure was usually manifested by an elevated central venous pressure (>20 mm Hg), a low left atrial pressure (<6 to 8 mm

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Table 1. Indications for Insertion of Ventricular Assist Device

	LHAD (Open)			
Indication	Nonsurvivors	Survivors	RHAD	Percutaneous LHAD
Inability to discontinue CPB	35	22	5	0
Preoperative cardiac arrest	11	8	1	2
Postoperative cardiac arrest	7	8	1	0
Cardiogenic shock after acute MI	0	0	1	5

CPB = cardiopulmonary bypass; LHAD = left heart assist device; MI = myocardial infarction; RHAD = right heart assist device.

Hg), systemic hypotension (systolic blood pressure <70 mm Hg), a low cardiac index (<1.5 L/min/m^2), and an elevated pulmonary vascular resistance. A trial of inotropic agents, pulmonary vasodilators, and systemic vasoconstrictors infused directly into the left atrium was usually attempted. An intraaortic balloon was also inserted in most patients. In 5 of the 7 patients, cardiopulmonary bypass could not be discontinued without the use of right heart bypass. In another patient, acute right coronary graft thrombosis occurred six hours postoperatively; after graft revision, a right heart assist device was inserted. An additional patient with a large inferior wall myocardial infarction sustained arrest during cardiac catheterization. This patient was placed on cardiopulmonary bypass, and a right heart assist device was inserted.

PERCUTANEOUS LEFT HEART ASSIST DEVICE. All 5 patients in whom a percutaneous left heart assist device was inserted were in profound cardiogenic shock after acute myocardial infarction (see Table 1). All patients had been given a trial of intensive medical therapy including coronary vasodilators, inotropic agents, and intraaortic balloon counterpulsation. Three of the 5 patients sustained cardiac arrest in the cardiac catheterization laboratory and could be successfully resuscitated only after insertion of the left heart assist device. Percutaneous transluminal coronary angioplasty was attempted in all patients and was successful in 4.

Preoperative Clinical Characteristics and Operations Performed

There were no major differences in the clinical characteristics of nonsurviving and surviving patients in whom a left heart assist device was inserted after a cardiac operation (Table 2). The types of operations performed were also similar in both groups as were the periods of aortic occlusion.

It has been our impression in the last few years that more of the patients who require a ventricular assist device postoperatively have arrived in the operating room in profound cardiogenic shock (eg, failed percutaneous transluminal coronary angioplasty, left main coronary artery dissection, evolving myocardial infarction, ruptured ventricular septum, ruptured papillary muscle).

Technique of Insertion

LEFT HEART ASSIST DEVICE. A 28F to 32F venous cannula is inserted through a pursestring suture into the left atrium through either the left atrial appendage or the right superior pulmonary vein. A 5- to 6-mm arterial cannula is inserted through a pursestring suture into the ascending aorta (Fig 1). The tip is advanced beyond the left subclavian artery to decrease the potential for cerebral embolization. Cannulas are brought out through the sternotomy

Table 2. Clinical Characteristics of Patients With Ventricular Assist Devices[a]

	LHAD			
Variable	Nonsurvivors	Survivors	RHAD	Percutaneous LHAD
Age (yr)	60.1 ± 2.0	59.8 ± 2.3	63.4 ± 3.1	69.7 ± 4.1
Preoperative cardiac index (L/min/m^2)	2.17 ± 0.1	2.34 ± 0.10	2.2 ± 0.1	1.3 ± 0.1
Ejection fraction (%)	40.7 ± 2.5	44.4 ± 2.6	38.5 ± 5.2	. . .
Operation				
CABG	31	24	3	. . .
AVR	5	0	0	. . .
AVR + CABG	0	3	0	. . .
CABG + LV aneurysm + closure of VSD	3	2	2	. . .
MVR + CABG	3	1	1	. . .
Acute RV infarction	0	0	1	. . .
Aortic cross-clamping (min)	66.7 ± 8.1	73.6 ± 9.6	52.3 ± 9.5	. . .
Cardiopulmonary bypass (min)	236.1 ± 22.8	228.1 ± 28.1	214.5 ± 30.6	. . .
Time on ventricular assistance (h)	36.4 ± 6.1	44.1 ± 4.6	68.3 ± 10.1	24 ± 16.5

[a] Where applicable, data are shown as the mean ± SD.

AVR = aortic valve replacement; CABG = coronary artery bypass grafting; LHAD = left heart assist device; LV = left ventricular; MVR = mitral valve replacement; RHAD = right heart assist device; RV = right ventricular; VSD = ventricular septal defect.

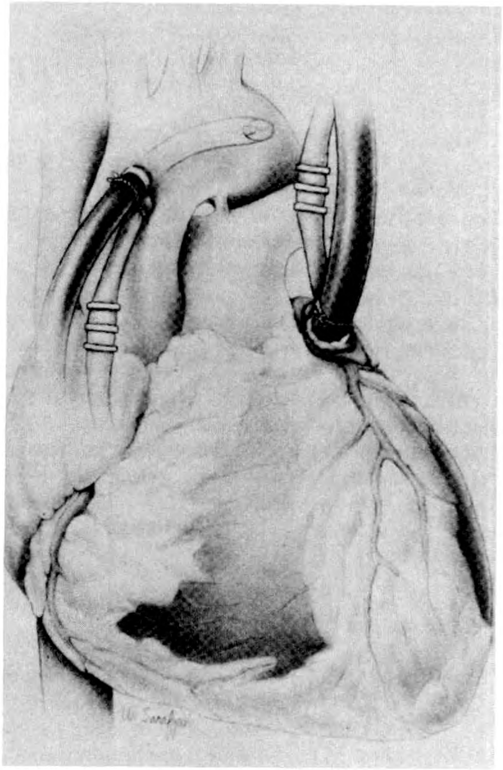

Fig 1. Intracardiac location of aortic and left atrial cannulas.

or through separate parasternal incisions (Fig 2). The cannulas are connected to 3/8 × 1/16-inch silicone tubing (Dow Corning Corporation, Midland, Mich), which is connected to a portable roller pump (Fig 3).

With this device, maximum flow rates of 3.5 to 4.0 L/min can be attained. After insertion of the left heart assist device, flow rates of 2.0 to 4.0 L/min are provided to maintain adequate systemic perfusion and discontinue cardiopulmonary bypass. Left atrial pressure is maintained between 5 and 12 mm Hg, inotropic agents are used to augment right heart function, and an intraaortic balloon is used to provide counterpulsation.

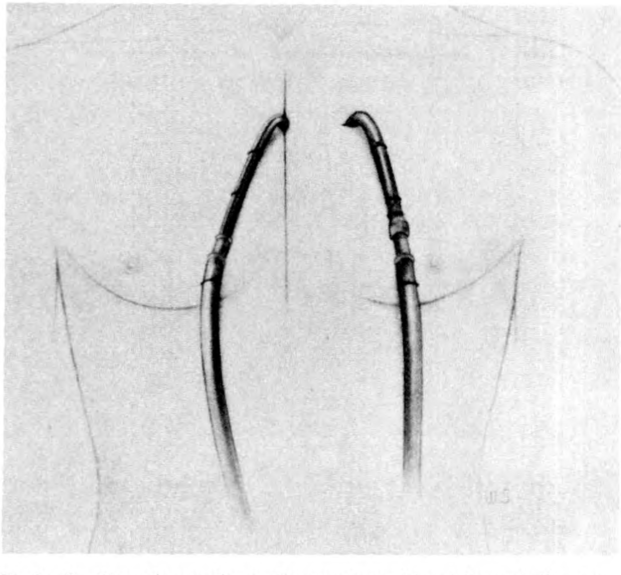

Fig 2. Position of cannulas as they are brought out through the sternum.

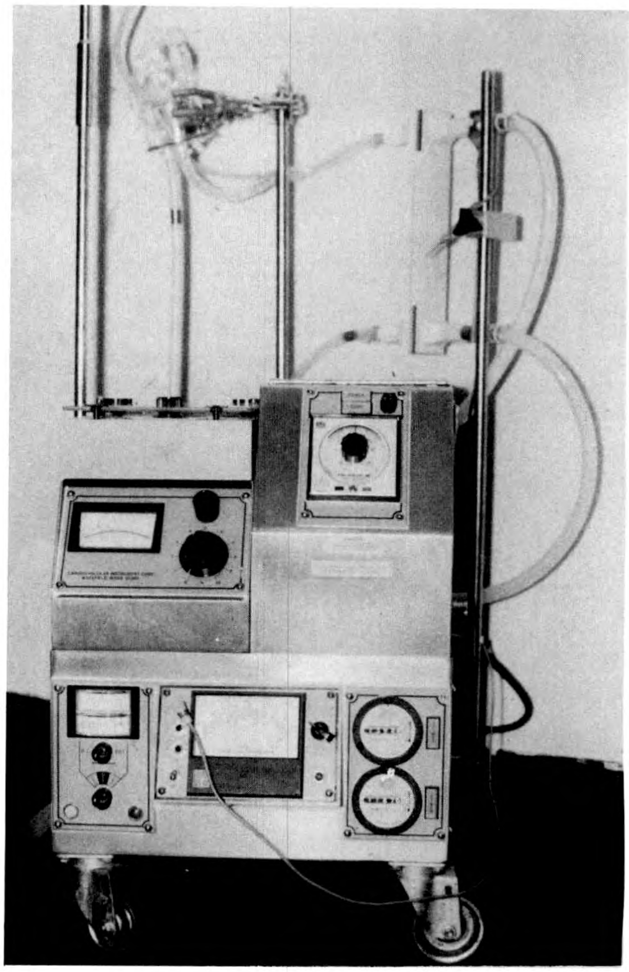

Fig 3. Portable roller pump that is employed for ventricular assistance.

When closing the chest, it is critically important to avoid cardiac compression and to open the pericardium widely. In some patients, the sternum cannot be closed without compressing the heart, and in these patients, it is necessary to leave the sternum open and close only the skin. In some patients it may not be possible to close the skin, and synthetic material can be used to cover the sternal defect.

The patient's heart rate, central venous pressure, pulmonary arterial pressure, left atrial pressure, and systemic pressures are all continuously monitored. Cardiac output is determined with a balloon-tipped thermodilution pulmonary artery catheter.

If postoperative bleeding is not great, patients receive 250 to 750 units of heparin per hour four to six hours after operation. The activated clotting time is maintained between 150 and 250 seconds with this regimen.

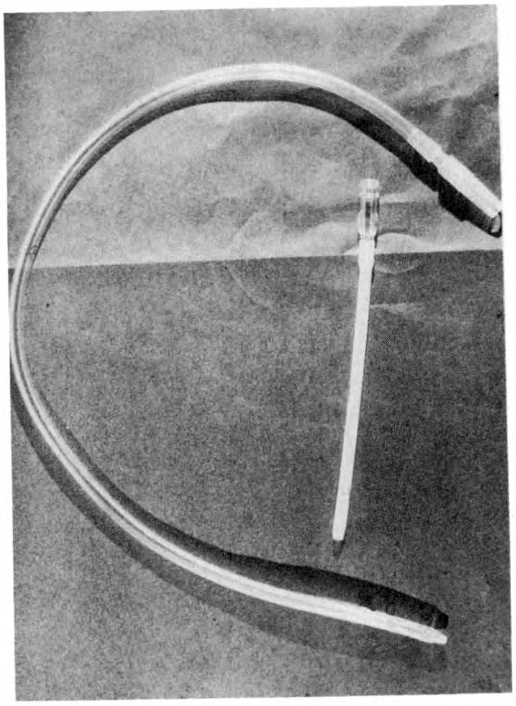

Fig 4. Percutaneous femoral arterial and left atrial cannulas.

RIGHT HEART ASSIST DEVICE. The technique for insertion of the right heart assist device is similar to that of the left heart assist device. A 28F to 32F venous cannula is inserted into the right atrium through a pursestring suture. A small arterial cannula is inserted into the main pulmonary artery through a pursestring suture. Cannulas are connected to the Silastic tubing (Dow Corning), which is then connected to a portable roller pump.

Flow rates of 2.5 to 4.0 L/min are employed. Similar precautions concerning pericardial constriction and sternal compression are observed. Patients are generally given pulmonary artery vasodilators and inotropic agents to enhance myocardial function. Vasoconstrictors can be infused through a left atrial line. Patients receive heparin in a fashion similar to that used with the left heart assist device.

PERCUTANEOUS LEFT HEART ASSIST DEVICE. A specially designed venous cannula (Electrocatheter Corp, Rahway, NJ) (Fig 4) is introduced through the femoral vein and passed fluoroscopically over a guidewire into the right atrium. Through a transseptal route, it is then introduced into the left atrium. Blood is returned to the patient with another cannula inserted into the femoral artery (see Fig 4). Flow rates of 1.5 to 3.0 L/min can generally be achieved with this system. In addition, inotropic agents and coronary vasodilators are given. Patients receive heparin as previously described.

Results

Left Heart Assist Device

Thirty patients (41.7%) were weaned from the left heart assist device 24 to 96 hours after insertion (Table 3, Fig 5). These patients had gradual recovery of left heart function, allowing gradual discontinuation of left heart bypass. Causes of death in the 42 patients who did not survive included severe coagulopathy, refractory arrhythmias, biventricular failure, and massive neurological injury. Often a combination of these factors was present and contributed to the death of the patient.

Table 3. Clinical Experience With Roller Pump Ventricular Assist Devices

Type	Total No. of Patients	Early Survivors	Late Survivors
Left heart assist device (open)	72	30 (41.7%)	21 (29.2%)
Right heart assist device (open)	7	2 (28.6%)	0
Left heart assist device (closed)	5	0	0

Nine patients died 21 to 90 days postoperatively, 7 as a result of sepsis and multisystem failure and 2 of pulmonary embolism. Two of the 21 long-term survivors died late, 4 months and 4 years postoperatively, both of cardiac causes. Of the 19 long-term survivors, 11 are in New York Heart Association functional class I, 7 are in class II, and 2 are in class III (Table 4). No preoperative or intraoperative patient factors appear to be predictive of survival.

Right Heart Assist Device

Two patients were weaned from the right heart assist device 48 and 72 hours after insertion (see Table 3). One patient died five days postoperatively of multisystem failure and sepsis, and the other died ten days postoperatively of pneumonia. Of the 5 patients who could not be weaned, 3 had profound coagulopathy, 1 had severe hypoxemia and "shock lung," and 1 had a massive neurological injury and subsequent discontinuation of right heart assistance. In 2 of these nonsurviving patients right heart assistance was prematurely discontinued. Shortly after removal of the device, there was a rapid

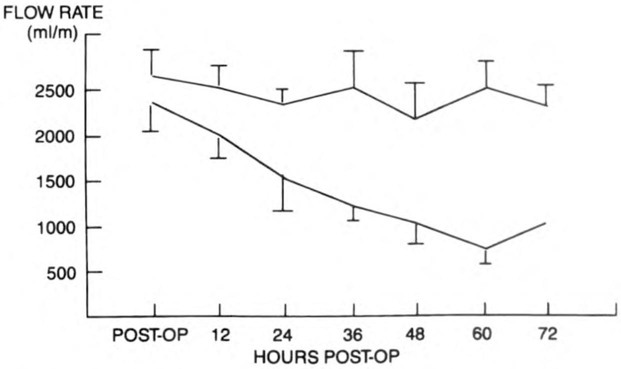

Fig 5. Flow rates of nonsurviving (upper line) *and surviving* (lower line) *patients. Note that there is improvement of ventricular function in many patients as early as 12 hours postoperatively.*

Table 4. Status of 30 Patients Weaned From LHAD

Status	No. of Patients
Early death (21–90 days)	
Pulmonary emboli	2
Sepsis (pulmonary, pancreatic, colon, renal)	7
Late death (4 mo; 4 yr)	
Sudden "cardiac" death	2
Long-term survivors	
NYHA class I	11
NYHA class II	7
NYHA class III	2

LHAD = left heart assist device; NYHA = New York Heart Association.

return of right heart failure, and the device had to be reinserted. Profound coagulopathy developed in both patients, and they died 72 and 96 hours postoperatively.

Percutaneous Left Heart Assist Device

No patient could be weaned from the percutaneous left heart assist device, although 4 patients did have successful percutaneous transluminal coronary angioplasty (see Table 3). Two patients died of refractory ventricular fibrillation two and four hours after insertion. One patient had a massive air embolus from the pump six hours after insertion. (This is the only patient in the entire series in whom this occurred.) Two patients died of progressive biventricular failure at 48 and 72 hours.

Comment

Left Heart Assist Device

Profound postoperative cardiac failure can be produced by multiple factors including previous myocardial infarction with depressed ventricular dysfunction, active ongoing ischemia or infarction, inadequate myocardial protection, and incomplete myocardial revascularization [10–12]. In addition, coronary artery vasospasm in the native coronary artery, vein graft, or internal mammary artery can produce severe myocardial failure and arrhythmias [13, 14].

It has been suggested that during the initial reperfusion period, there is an imbalance in oxygen supply and demand, and that despite adequate reperfusion, there may be cellular and metabolic abnormalities that could impair ventricular function [15, 16]. This would cause the myocardium to act as if it had been "stunned," as suggested by Braunwald and Kloner [17]. As this group of investigators [16] has shown, acute coronary artery occlusion for only 15 minutes can result in functional and metabolic abnormalities for as long as seven days. Thus, despite adequate revascularization, some patients can have persistent cardiac failure as a result of the myocardium being stunned.

Previous experimental studies indicate that left ventricular bypass and left atrial bypass can both effectively unload the left ventricle and arrest infarct expansion [9, 18, 19]. Thus, marginally perfused ischemic tissue that could ultimately be involved in the infarct can be salvaged with the use of left heart bypass. A critical determinant of survival is the extent of irreversibly infarcted tissue compared with the amount of reversibly injured ischemic tissue, and this ratio can be favorably affected with the use of left heart bypass.

The optimal or necessary period of left heart support has not been clearly defined. The device we have employed is not capable of providing flow rates as high as those of the device used by Pae and associates [2]. With the device we have used, surviving patients will demonstrate evidence of left ventricular recovery as early as 12 hours postoperatively, and most surviving patients will show improvement in left ventricular function within 48 hours postoperatively (see Fig 5) [1, 9].

We have been reluctant to maintain flow rates in excess of 3,000 mL/min for prolonged periods in our patients because we thought that this could produce substantial hemolysis and destruction of blood elements. However, if larger arterial and venous cannulas were inserted, these problems most likely would not occur. The group in Hershey, Pa [2], has supported patients with their left heart assist device for as long as 25 days (mean, 6.8 days). Thus, the optimal period of left heart support varies considerably with the type of assist device employed. The device Pierce and co-workers have used is capable of providing flow rates of up to 6.5 L/min. Therefore, it seems that with more complete left heart bypass, patients can be successfully supported for longer periods.

Right Heart Assist Device

The causes of right heart failure are similar to those of left heart failure (eg, active ongoing ischemia or infarction, inadequate myocardial protection, incomplete revascularization, vasospasm) [20–22]. In addition, right heart failure can be exacerbated or caused by increased pulmonary vascular resistance [23]. Often a combination of these factors (right heart ischemia and elevated pulmonary vascular resistance) will be present. Although we have not had any experience with pulmonary artery balloon counterpulsation, there have been some encouraging results with this technique [24, 25].

The effects of right heart bypass on pulmonary microcirculation and lung water formation have not been clearly elucidated experimentally. Some recent experimental data suggest that right heart bypass may have a deleterious effect on pulmonary function. Thus, the right heart support device could, in some instances, create further pulmonary injury and elevate pulmonary vascular resistance, further impairing right heart function.

It is evident from experimental and clinical data that the right heart can often recover sufficiently to permit removal of the support device [2, 20, 21]. However, we have observed a quite dramatic counter to this. In 2 patients in this series, there was premature discontinuation of the right heart assist device, and this resulted in the insidious return of profound right heart failure and cardiac arrest. The recurrence of right heart failure may be a result of an increase in pulmonary vascular resistance that has gone undetected.

Clearly, in many patients there is evidence of biventricular failure [5]. However, the failure is often predominant in one chamber, and thus either a right or left heart assist device can be successfully employed. Our experience with biventricular assistance is minimal. However, based on the experience of others, it does seem that patients with severe biventricular failure will generally go on to cardiac transplantation if they are suitable candidates [2, 8].

Percutaneous Left Heart Assist Device

The results with the percutaneous left heart assist device have been poor. However, we are still in the early phases of the development of this technique. All of the patients in whom the device was employed were extremely ill; they were either in profound cardiogenic shock or having active cardiac arrest. As we gain further experience and expertise, this technique probably can become a useful adjunct in patients with acute evolving myocardial infarction and potentially reversible left ventricular dysfunction.

Conclusion

As our results indicate, reasonably good results can be achieved with a roller pump type of ventricular assist device. Further experience in treating patients with acute evolving myocardial infarction must be obtained. In the future, further refinement of all existing assist devices will be necessary to make them less complicated and more economical, and enhanced patient survival will be mandatory if they are to gain widespread use.

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Use of the Pierce–Donachy Ventricular Assist Device in Patients With Cardiogenic Shock After Cardiac Operations

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In spite of recent improvements in cardiac surgery, a small percentage of patients have severe postcardiotomy ventricular failure refractory to drugs and the intraaortic balloon. In our experience, the Pierce–Donachy external pneumatic ventricular assist device has proved to be one of the most effective devices for these patients. Since 1981, 30 patients aged 15 to 71 years (mean age, 52 years) with profound cardiogenic shock refractory to conventional therapy after cardiotomy were supported with the Pierce–Donachy ventricular assist device. Fourteen required left ventricular support, 7 needed right ventricular support with an intraaortic balloon, and 9 had biventricular assistance. Duration of support ranged from three hours to 22 days (mean length, 3.6 days). Seven of the first 11 patients seen died in the operating room of bleeding, biventricular failure, or both. However, 16 patients (53%) had improved cardiac function, 15 (50%) were weaned, and 11 (37%) were discharged. Of the last 19 patients in the series, 47% survived. Factors affecting survival were myocardial infarction (75%) and renal failure (90%). Common complications were bleeding (73%) and biventricular failure (83%).

(Ann Thorac Surg 1989;47:130–5)

Successful application of mechanical circulatory support in patients with cardiogenic shock after cardiac operation was done in the mid-1960s by Spencer and associates [1] and DeBakey [2]. Recently, postcardiotomy circulatory support has been accomplished successfully in many patients with a variety of systems, including roller pumps [3], centrifugal pumps [4], and sac-type pneumatic pumps [5]. At St. Louis University, we have employed these devices for a variety of problems, but patients with profound cardiogenic shock after cardiotomy continue to present our greatest challenge. It is now apparent that our best results have been with the Pierce–Donachy ventricular assist device (VAD) designed by Pierce and Donachy at Pennsylvania State University [6].

This report analyzes our experience with the Pierce–Donachy VAD in postcardiotomy patients over the last 7 years, and attempts to establish guidelines for appropriate application of the device.

Material and Methods

Description of the Device and Technique for Insertion

The Pierce–Donachy VAD (Thoratec Corp, Berkeley, Calif) is a paracorporeal pneumatic sac-type device constructed of a machined polycarbonate housing with an angle-port design containing a flexible, seam-free segmented polyurethrane sac (Fig 1). The VAD utilizes Björk–Shiley inlet and outlet valves and has a stroke volume of 65 mL with a dynamic ejection fraction of approximately 0.75. An inlet cannula for the atria, a left ventricular cannula, and an outlet cannula that can be used for the aorta or pulmonary artery are available. The atrial cannula is a 51F Sarns venous cannula coated with polyurethane (Biomer) and shaped to a right-angle configuration. The left ventricular apex cannula and the aortic cannula are large-bore, wire-bound, segmented polyurethane (Biomer) tubes. A Dacron graft forms the end of the infusion cannula, thus permitting a standard vascular anastomosis to the aorta or pulmonary artery. The ventricular cannula is fitted with a felt washer to permit suture fixation to the ventricular myocardium. This cannula system allows cannulation of the left ventricle, the left and right atria, and the aorta or the pulmonary artery (Fig 2).

The pneumatic power control unit (Thoratec) is capable of functioning in three modes: a manual set-rate mode, a synchronized mode that detects the R wave of the electrocardiogram, or a fill-to-empty mode that operates by activating a Hall effect switch when the sac is full, thus initiating the emptying cycle. When the VAD is operating in the fill-to-empty mode, the rate times the stroke volume (65 mL) equals VAD flow.

To avoid injury to left ventricles that we hoped would recover, patients underwent left atrial cannulation by placement of the cannulas through pursestring sutures in

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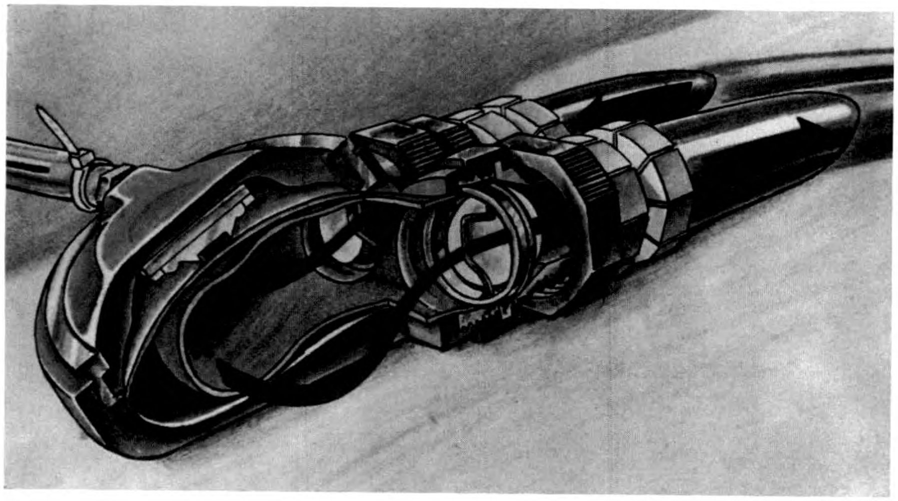

Fig 1. Cross-sectional view of Pierce–Donachy ventricular assist device.

the left atrial appendage, the dome of the left atrium, or just anterior to the entrance of the right pulmonary veins. Right-sided VAD inflow cannulas were placed into the right atrium through pursestring sutures. The VAD outflow cannulas were preclotted and sutured to the main pulmonary artery or aorta. The VADs were all inserted during cardiopulmonary bypass (CPB).

In 3 patients with left-sided Pierce–Donachy pumps, right heart bypass was accomplished with a Bio-Medicus centrifugal pump (Bio-Medicus, Eden Prairie, Minn) connected to the patient by Tygon tubing (Norton Inc, Akron, Ohio). Standard USCI CPB venous cannulas (William Harvey, Santa Ana, Calif) were used. The right atrial cannula was placed through a pursestring suture, and the pulmonary artery cannula was placed through a No. 14 woven Dacron graft sutured to the pulmonary artery.

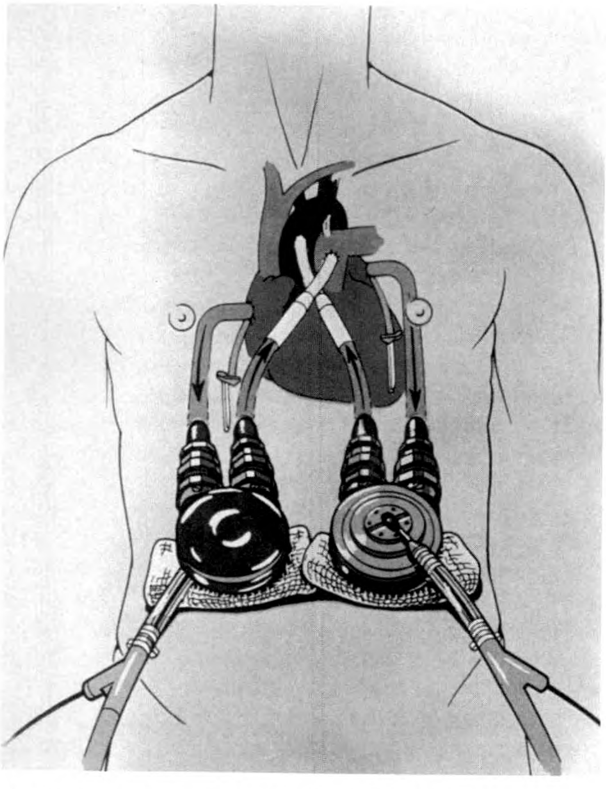

Fig 2. Biventricular assist devices showing atrial cannulation.

Patient Selection

All patients in the series met a predetermined set of hemodynamic criteria derived from the studies of Norman and associates [7], and adopted by the clinical investigation group of the National Heart, Lung, and Blood Institute [8]. Patients were chosen who, in spite of optimal preload levels, maximum inotropic support, and intraaortic balloon (IAB) support, were unable to maintain the following: cardiac index greater than 1.8 L/min/m^2; systemic vascular resistance lower than 2,100 dyne-s/cm^5; systolic blood pressure greater than 90 mm Hg; right and left atrial pressures lower than 20 mm Hg; and urine output greater than 20 mL/h. Patients who fail to meet these basic hemodynamic criteria for more than 12 hours have an extremely high mortality [7]. From April 1981 to August 1988, we encountered 30 patients aged 15 to 71 years (mean age, 52 years) who failed to meet these minimum hemodynamic criteria in spite of conventional therapy, including the IAB pump (29 patients).

Hemodynamic variables, including right and left atrial pressures, thermodilution cardiac output, mixed venous oxygen saturation, and systemic arterial pressure, were measured before and after implantation of the VADs. Determination of perioperative myocardial infarction was made by analysis of serial electrocardiograms and lactate dehydrogenase and creatine kinase isoenzymes. Ventricular function was assessed by hemodynamic measurements, radionuclide imaging, and echocardiography. Radionuclide imaging of the ventricular function in patients with a VAD required some modifications of established nuclear medicine techniques as previously described [9]. Pathological examinations of the sacs and cannulas were made by gross inspection and light and electron microscopy. Patients who died underwent complete postmortem examination according to a protocol that included myocardial staining for infarction. In a few patients, right ventricular needle biopsies were done at the time of insertion and removal of the devices. Approximately 1 month after removal of the VAD, survivors were evaluated by echocardiography, nuclear ventriculography multigated acquisition, or cardiac catheterization.

In all patients, anticoagulation with heparin sodium was used during CPB for pump insertion. As soon as patients were weaned from bypass with VADs, full reversal of heparin with protamine sulfate was accomplished. Heparin was not used again until the weaning process was begun. Eight postcardiotomy patients who died in the operating room received no anticoagulants at all; 22 patients received low molecular weight dextran at 25 mL/h.

Our previous experience [10] suggested that biventricular failure was a common problem in postcardiotomy failure. The diagnosis of predominant left or right ventricular failure was initially made when one ventricle appeared to be contracting less well and its associated atrial pressure exceeded the filling pressure of the other ventricle. In the absence of these findings, balanced ventricular failure was judged to be present. All patients without severe peripheral vascular disease underwent initial placement of an IAB, whether the failure was considered to be predominantly right or left. As these studies evolved, we became more aware of the frequency of biventricular failure and the importance of mechanical support for both ventricles in such instances. In several patients, temporary left or right heart bypass was established using the standard CPB system to determine whether the other ventricle could function without a VAD.

When the patient had been in stable condition on the VAD for at least 24 hours, the VAD flow was interrupted for two to three minutes to determine pump-on/pump-off hemodynamic data. During the course of these studies, it became apparent that clamping of the cannulas during periods when the pump was off promoted thrombosis. As a result, the cannulas are no longer clamped during pump-off periods. Pump-on/pump-off data were rarely obtained prior to 24 hours of VAD perfusion because in most patients ventricular recovery was not adequate to support the circulation. During weaning, the pump rate was gradually decreased to a level of 40 beats per minute by one of two methods: reducing the rate in the manual mode or setting the VAD rate at 1:2 or 1:3 in the electrocardiogram synchronized mode. Simultaneously, intravenous administration of heparin was begun to maintain the activated clotting time at one and a half times the control value. If satisfactory pump-off data were obtained 12 to 24 hours after the weaning process was begun, the patient was returned to the operating room for repeat sternotomy and removal of the device. We [11] have previously described our most effective predictors for weaning patients from VADs.

Results

Of 4,696 patients undergoing cardiac operations at St. Louis University Hospital from February 1982 to August 1988, 30 patients aged 15 to 71 years (mean age, 52 years) were treated with Pierce–Donachy VADs. The cardiac operations were performed during standard CPB. In 1 patient, the aorta was not clamped. The aortic clamp times in 29 patients ranged from 30 to 156 minutes (mean time, 83 minutes). One patient was maintained on extracorporeal membrane oxygenation in the operating room for 12 hours before insertion of a right VAD. Four patients had IABs inserted preoperatively, 25 patients had IABs inserted during operation, and 1 patient had severe peripheral vascular disease, which prohibited IAB placement.

Table 1. Diagnosis in 30 Patients

Diagnosis	No. of Patients
Coronary artery disease	17
Mitral valve disease and/or coronary artery disease	6
Left ventricular aneurysm and/or coronary artery disease	3
Congenital heart defect	2
Ascending aortic aneurysm	1
Prosthetic valve endocarditis	1

As expected, coronary artery disease, with or without ventricular aneurysm, was the most frequent diagnosis (Table 1). Mitral valve replacement was necessary in 6 patients (with or without coronary artery disease), most of whom required biventricular support. One 28-year-old man with Down's syndrome had a septum primum atrial septal defect, cleft mitral valve, and unrecognized hypoplastic left ventricle. A 27-year-old woman with a septum secundum atrial septal defect and anomalous right pulmonary veins may have sustained coronary air embolization in spite of measures to prevent it. Another patient underwent aortic valve replacement for prosthetic valve endocarditis and aortic insufficiency, and 1 patient had replacement of an ascending aortic aneurysm. All patients met our criteria for severe ventricular failure modeled after the studies of Norman and associates [7] for patients with cardiogenic shock who are on IAB support and have optimal preload levels.

The VAD was inserted in 20 patients because they could not be weaned from CPB. Eight patients were initially weaned from CPB but sustained cardiac deterioration in the operating room and required reinstitution of CPB and VAD replacement. One patient was maintained on partial CPB for 12 hours until a right VAD was inserted. The condition of another patient deteriorated six hours postoperatively in the intensive care unit, and the patient was returned to the operating room for insertion of a left VAD. All patients were eventually weaned from CPB with maximum VAD flows ranging from 1.6 to 2.9 L/min/m^2. The length of VAD perfusion was less than 12 hours in 9 patients, between one and seven days in 15 patients, and greater than seven days in 6 patients.

Bleeding, biventricular failure, and multiple-organ failure accounted for the deaths of 14 patients who had no improvement in cardiac function. Sixteen patients (53%) demonstrated improvement in cardiac function, 15 (50%)

Table 2. Complications in 30 Patients

Complication	No. of Patients
Biventricular failure	24
Bleeding	22
Respiratory failure	10
Renal failure	10
Dialysis	9
Infection	8
Thrombus	3
Embolus	0
Neurological deficit	2
Cerebrovascular accident	2
Hemolysis (plasma hemoglobin > 40 mg/dL)	2
Mechanical failure	1
Intraaortic balloon pump (limb ischemia)	1

were weaned from the VAD, and 11 (37%) were discharged from the hospital. Although 7 of the first 11 patients in the series died in the operating room, there was only 1 intraoperative death among the last 19 patients. Sixty-three percent of the last 19 patients were weaned, and 47% (9 patients) survived. Of the 11 survivors followed 6 to 60 months after hospital discharge, 1 died of severe cardiomyopathy 6 months after discharge, 1 died 26 months after discharge of unknown causes, and 1 died of metastatic cancer 53 months after discharge. Four patients returned to work or school, 2 retired, 1 is recovering, and 1 has recurrent episodes of congestive heart failure but refuses further treatment.

Biventricular failure occurred more commonly than isolated ventricular failure (Table 2). Of the 30 patients, 14 received only a left VAD, 7 received only a right VAD (with an IAB to support the left ventricle), and 9 received biventricular assist devices. Eight of the 16 patients who received biventricular support were weaned, and 6 were long-term survivors. In contrast, of 8 patients with biventricular failure who received only a left VAD just 2 were weaned (25%) and 1 survived. Of 6 patients with isolated left ventricular failure, 5 received only a left VAD and survived. The sixth patient died in the operating room of a tear in the left atrium. In 2 of the 4 surviving patients with a left VAD, minimal use of inotropic drugs was required during the period of full left VAD support. In the other 2, inotropic drugs were not required until the weaning process was begun.

Bleeding led to at least one reoperation in 18 of the 30 patients (see Table 2), two reoperations in 2 patients, and four reoperations in 2 patients. Early in our experience, we left the sternum open and closed only the skin, a technique that facilitated reoperation in the intensive care unit. In the latter part of the study, we found that sternal closure decreased the amount of bleeding and allowed for endotracheal tube removal. Disseminated intravascular coagulation was documented in only 1 patient; coagulation disorders in the other patients were of diverse etiology. Hemolysis (plasma hemoglobin level > 40 mg/dL) occurred in 2 patients, but cleared during the course of VAD perfusion, suggesting that hemolysis was unrelated to the VAD. Maximum plasma hemoglobin levels per patient ranged from 5 to 139 mg/dL (mean value, 15 mg/dL).

Thrombus was noted in three VAD sacs. In 1 patient with biventricular assist devices, we had intermittently clamped the right VAD cannulas to perform thermodilution cardiac output measurements. At the time of right VAD removal, there was a large thrombus (3 × 4 cm) in the right VAD sac and small thrombi on the right VAD valves. The other 2 patients had small thrombi (less than 3 mm in diameter) firmly adherent to the VAD sac. We subsequently discontinued the practice of briefly clamping the cannulas during pump-on/pump-off periods, and have had no visible thrombi present in the last 18 postcardiotomy patients who were perfused from eight to 528 hours. After 48 to 72 hours, a thin, fibrous layer composed largely of acellular elements forms on the sac and can be gently lifted away at the time of VAD removal.

In spite of the finding of thrombus in some sacs, there were no documented instances of embolism from the sacs. Two patients had strokes during the perioperative period. In 1 of them, the postoperative course was complicated by renal failure, sepsis, and a large right-sided stroke. The etiology of the stroke was never determined because both the left and right VAD sacs were free from thrombus at removal. The second patient sustained a stroke of the left parietal lobe during the weaning period. Both VAD sacs were free from thrombus at the time the device was removed. However, as the patient sustained the stroke during the period of lowest flow, it is possible that the stroke was related to the device. The patient regained full function of his extremities within 6 months and was working full-time within a year of discharge.

Postmortem examinations were performed on 15 of the 19 patients who died during the immediate postoperative period. Eleven patients had evidence of extensive myocardial infarction, which occurred during the perioperative period (Table 3). Five of these patients were known to have sustained acute myocardial infarctions preoperatively, which led to acute cardiogenic shock necessitating emergency cardiac operations. One patient had an extensive myocardial infarction during bypass grafting. Two

Table 3. Survival Among Patients With Myocardial Infarction

Myocardial Infarction	Survivors	Nonsurvivors
Proven (autopsy or ECG and enzymes)	1	11
Likely (positive ECG or enzymes)	2	1
Possible (inadequate data)	1	3
None	7	4
Total	11	19
Incidence of infarction (%)[a]	27	63

[a] This is based on proven or likely diagnosis of myocardial infarction.

ECG = electrocardiogram.

patients without acute myocardial infarctions had evidence at autopsy of either diffuse ischemic changes or focal interstitial myocarditis. Four patients did not have a postmortem examination. In 2 of them, right ventricular biopsy specimens demonstrated myocardial necrosis; 1 died in the operating room of a tear in the left atrium and the other of biventricular failure. Based on these pathological data, we estimated that at least 11 patients had myocardial injuries that in themselves were severe enough to preclude survival. The deaths of the other 8 patients were attributed primarily to bleeding, biventricular failure, and renal failure.

Of the 11 survivors, 3 had some evidence of perioperative myocardial injury. One patient had elevated cardiac enzyme levels but no changes from the preoperative electrocardiogram, and 1 patient had electrocardiographic evidence of an infarction but normal postoperative enzyme levels. The latter patient lived for 6 months after discharge and then died of extensive myocardial infarctions in spite of patent coronary arteries. Only 1 discharged patient had positive electrocardiographic and enzymatic changes clearly indicating a perioperative acute myocardial infarction. Ten of the 11 survivors underwent echocardiographic or nuclear angiographic multigated acquisition evaluation approximately 1 month after operation. The left ventricular ejection fractions ranged from 32% to 72% (mean value, 53.5%), and 8 patients had normal ejection fractions.

Comment

This series demonstrates the increasing success of mechanical support of the failing ventricle after cardiac operations. Although our survival of 37% is not as high as desired, it has gradually improved. Seven of our first 11 patients died in the operating room, but of the subsequent 19 patients, 63% were weaned and 47% survived. We attribute our increasing success to improved patient selection, earlier application of devices, better control of postoperative bleeding, and more aggressive treatment of biventricular failure.

Fifty-three percent of our patients required biventricular support: 9 received biventricular assist devices and 7 were supported with right VADs and IABs. The rate of weaning and the survival in the 16 patients who received biventricular support were substantially better than the results in patients with biventricular failure who received mechanical support of the left ventricle only. However, of the 6 patients with isolated left ventricular failure who received only a left VAD, 5 were weaned and survived (83%), thus indicating that some VAD candidates do not require biventricular devices. Isolated left ventricular failure does occur, and it can be treated effectively with a left VAD alone [10].

We continue to prefer left atrial cannulation for patients with postcardiotomy heart failure to avoid injury to the left ventricle. Although Bernhard and co-workers [12] were successful with ventricular recovery after apex cannulation, we believe left atrial cannulation allows the ventricle more potential for recovery. Although apex cannulation allows for better ventricular decompression, it is apparent that ventricular recovery can occur without complete decompression, as evidenced by our results utilizing atrial cannulation.

Two important factors are strong negative determinants of survival: perioperative myocardial infarction and renal failure [13, 14]. Bleeding was a frequent problem in these patients, who had all undergone cardiac operations and periods of CPB. In spite of complete reversal of heparin anticoagulation with protamine, postoperative bleeding was frequent. Although disseminated intravascular coagulation was rarely documented, many patients have platelet disorders and other coagulation defects [15]. In the latter part of the study, we wired the sternum when possible, and the bleeding seemed to decrease. Meticulous surgical technique, the withholding of heparin, and liberal administration of platelets and fresh frozen plasma seem to have also helped decrease the incidence of bleeding.

In 1987, we [13] reported the important effect of a perioperative myocardial infarction on survival of VAD patients, and our present data support that thesis. Of the 11 survivors in this series, only 1 had clear evidence of a perioperative infarction, whereas 11 of the 19 nonsurvivors had acute myocardial injuries severe enough to preclude survival. Previously, we [10] demonstrated that preoperative left ventricular function was not as important in determining survival as the effects of biventricular failure or perioperative infarction. Considering our present series, it continues to appear that acute perioperative myocardial infarction is an important negative determinant of survival.

Renal failure requiring dialysis is also an important factor influencing survival. In this series of 30 patients, renal failure developed in 10 patients, 9 of whom had dialysis; there was 1 survivor. In an earlier evaluation of 27 VAD patients at our institution [14], 13 of 15 nonsurvivors had renal failure. It is clear that renal failure requiring dialysis in our VAD patients was highly predictive of death.

Infection in patients with VADs is also an important event that can influence survival [16]. In this series, infections developed in 8 patients, pneumonia in 7 patients and empyema in 1 patient. Mediastinitis developed in 2 patients who had undergone multiple sternotomies for bleeding complications. Only 1 of the 8 patients with a major infection survived. All organisms isolated were typical nosocomial pathogens and not opportunistic agents. Surprisingly, the cannula exit sites were frequently uninvolved with infection and when infection did occur at the cannula sites, mediastinitis was not inevitable. Duration of support appears to be a factor in the development of infection; hence, weaning should be initiated after the first 24 hours of stabilization. Previous studies [11] suggested that hemodynamic measurements of atrial pressures and cardiac index with the VAD off were predictive of successful weaning. Therefore we perform pump-on/pump-off measurements as soon as the hemodynamic data suggest that weaning might be successfully accomplished.

Of the 11 patients discharged, 3 died. Only 1 of these deaths was cardiac related. The survivors are leading active lives, and many have returned to work or school. Follow-up studies demonstrate normal or nearly normal ventricular function in more than half of the recipients. It is now apparent that many patients with postcardiotomy failure have a stunned myocardium that can undergo full recovery [8, 17]. The Pierce–Donachy VAD has proved to be an effective device for postcardiotomy patients, and salvage rates are increasing as we improve patient selection and device applications.

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SWAT Team Approach to Ventricular Assistance

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In 1986, the Cardiovascular Research Institute in Sion, Switzerland, created a flying bridge-to-cardiac transplantation team. This team, consisting of two physicians, a physicist, a biomedical engineer, and two intensive care nurses, has participated in 23 bridges to cardiac transplantation in 11 cardiovascular surgery centers in Europe. The cardiac function of all patients was 100% supported by paracorporeal pneumatic biventricular Pierce–Donachy devices. Twenty of the 23 patients have had transplantation, and 11 are alive and well. The bridge-to-cardiac transplantation team, which travels with a transportable driver and the ventricle sets, supervises the bridged patients 24 hours a day until cardiac transplantation is performed.

(Ann Thorac Surg 1989;47:136–41)

The Cardiovascular Research Institute was created in 1985 in Sion, Switzerland. The two major activities of this institute are the realization of a totally implantable electromechanical artificial heart and the clinical application of the Pierce–Donachy ventricular assistance device (VAD) as a bridge to cardiac transplantation. The Cardiovascular Research Institute is not directly connected with a specific cardiac surgery center, and it offers its services to any European transplantation center needing support for a bridge-to-cardiac transplantation procedure.

This report describes the organization of the bridge-to-transplantation team (BTT) of the Cardiovascular Research Institute, and summarizes the 23 cases of bridging to cardiac transplantation in which the BTT has collaborated in Europe.

Material and Methods

Organization

A multidisciplinary team consisting of an anesthesiologist, a cardiologist, a biomedical engineer, a physicist, and two intensive care nurses is on call 24 hours a day. Furthermore, a cardiac surgeon is at the disposal of the BTT in case the intervention takes place in a center that has no experience with the surgical implantation of the device. The BTT has the capability to provide, on short notice, clinical services for mechanical assistance to a failing heart in any properly equipped cardiac transplantation center in western and central Europe.

The materials used are the Pierce–Donachy (Fig 1) VAD and a Thoratec driver (Fig 2) modified by the Cardiovascular Research Institute so as to be transportable in a car or a small airplane. A typical clinical set consists of three pumps and the corresponding cannulas. In general, two pumps are used for a bridge-to-cardiac transplantation operation, and the third is a spare pump in case a major problem arises with one of the devices during its implantation.

During working hours, the team can be reached at the Cardiovascular Research Institute. Otherwise, during nights and holidays, the BTT can be reached through a permanent telephone service and a beeper system (Fig 3) that allows the BTT to contact the calling transplantation center and get ready for the intervention.

The calling center has to be an approved center for cardiac transplantation with a certain level of experience in the field. The BTT will base its acceptance on clinical information provided with the initial request for services. This information includes the following:

Age, sex, and blood group of the patient.
Confirmation that the patient is accepted as a transplant candidate.
Diagnosis, ie, type of cardiac pathological process.
History:

1. The clinical variables including the patient's central nervous system status, chest roentgenogram, and urinary output within the last eight hours. We also need to know if the patient is intubated, if he or she had one or several cardiac arrests in the last 24 hours, and what the current cardiac supports are (drugs and means of mechanical support, if any).
2. The hemodynamic variables including right atrial, pulmonary artery, left atrial or pulmonary wedge, and arterial pressures and cardiac output.
3. The metabolic variables including serum bilirubin, serum creatinine, and hepatic enzyme levels, prothrombin time, partial thromboplastin time, activated coagulation time, plasma hemoglobin level, hematocrit, platelet count, partial pressures of arterial oxygen and carbon dioxide, and arterial pH.

Furthermore, for the perioperative monitoring of the patient, we request a direct arterial pressure line, a Swan–Ganz thermodilution catheter for pulmonary arterial pressure, central venous pressure, pulmonary wedge pressure, and cardiac output measurements, and a urinary

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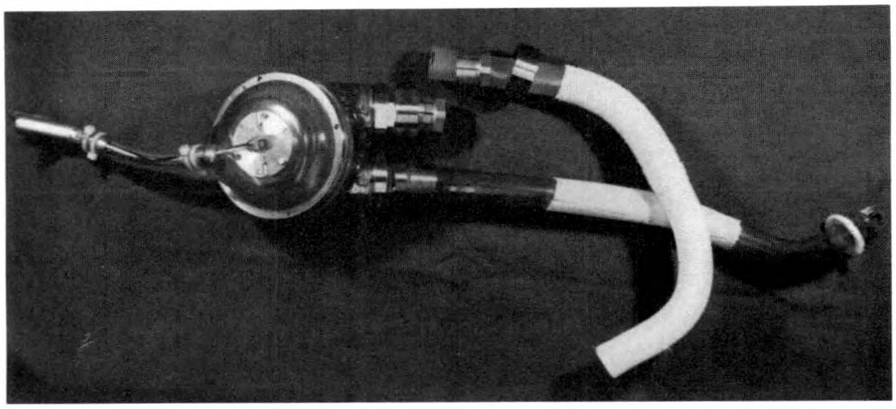


Fig 1. Pierce–Donachy ventricular assist device.

catheter. For the visual display, one oscilloscope is needed for three pressure traces and one electrocardiogram.

We request that the patient stay in an isolated intensive care unit for the time of the whole bridging procedure and that accurate prevention of infection is accomplished as for transplant patients.

The mean response time between the moment when the final decision is made and the arrival of the BTT at the destination has been about two and a half hours. This does not include the call from Portugal; five hours were necessary for that service. The BTT needs less than 15 minutes from the time of arrival at the hospital to get all of the equipment ready in the operating theater. After the implantation of the devices, the BTT assumes the continuous supervision of the patient and the assistance system. An anesthesiologist, a biomedical engineer, and an intensive care nurse of the BTT are available 24 hours a day during the whole bridging period.

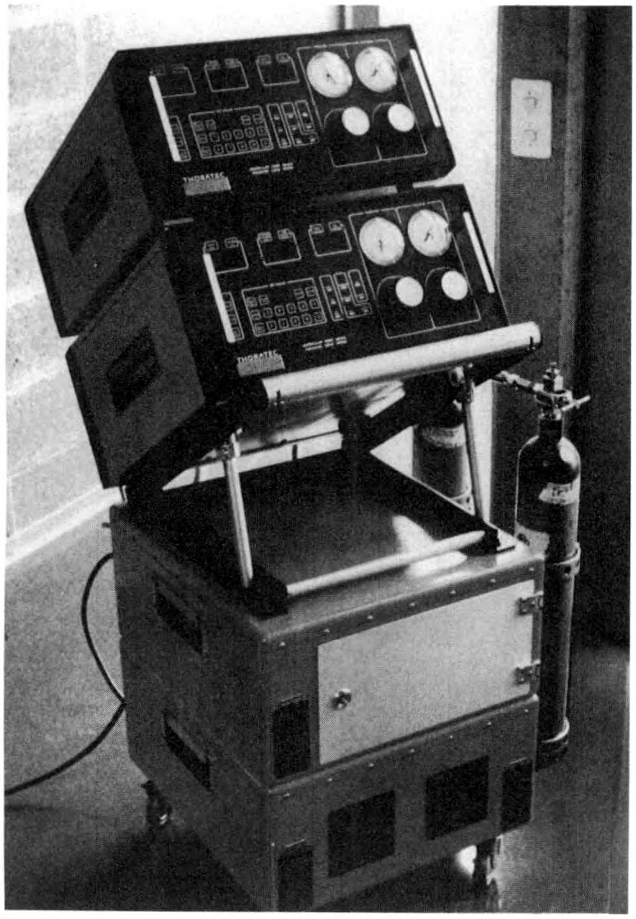


Fig 2. Thoratec transportable driving unit as modified by the Cardiovascular Research Institute.

Patient Selection

Since February 1986, we have received 40 calls. Fifteen cases were not accepted by the BTT: 4 cases were refused because the BTT was involved in another center, 2 procedures could not be performed because the VADs were not delivered in time, and 9 cases were considered outside the protocol. Twenty-five cases were accepted as being suitable for a bridging procedure. In two instances, the implantation of the device did not take place; 1 patient had a myocardial carcinoma that was too far advanced, and the other patient died before the arrival of the BTT.

Twenty-three patients have been assisted by the bridge-to-cardiac transplantation procedure in 11 different cardiac surgery centers in France, Germany, Italy, and Portugal (Fig 4). Ten patients had end-stage dilated cardiomyopathy, 6 had an acute myocardial infarction, 4 had ischemic cardiomyopathy, and 1 each had a postinfarction ventricular septal defect, a malfunction of a transplanted heart, and a left ventricular aneurysm. There were 20 male patients, ranging in age from 17 to 58 years (mean age, 44 years), and 3 female patients, ranging in age from 26 to 57 years (mean age, 38 years).

All patients were receiving maximum inotropic drug support. Eight patients were supported by an intraaortic balloon pump and 3 by femorofemoral circulatory assistance with a roller pump and a membrane oxygenator. Twelve patients were intubated and ventilated. Only 11 patients were conscious before implantation of the VAD. The mean urinary output of all the patients was 327 mL during the eight hours preceding the implantation of the device.

Operative Procedure

Implantation is effected through a median sternotomy. The cannulas for left ventricular assistance are first im-

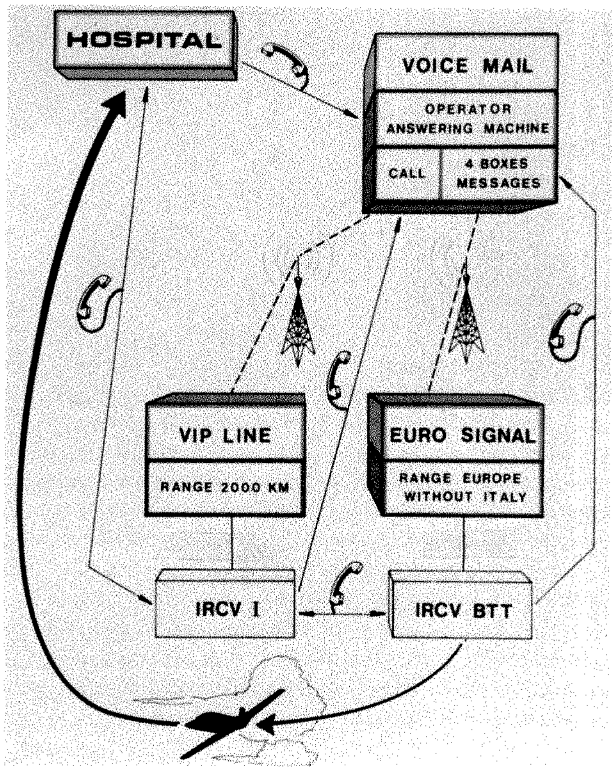


*Fig 3. Emergency call system of the Cardiovascular Research Institute (*IRCV*). (*BTT = *bridge-to-transplantation team.)*

planted. The left atrial cannula is introduced from the right side of the heart through the interatrial groove (19 patients) or the roof of the left atrium (4 patients), and the Dacron of the aortic cannula is sewn by a side-to-end anastomosis onto the ascending aorta. For right ventricular assistance, the atrial cannula is introduced through the right atrial appendage, and the pulmonary cannula is sewn onto the pulmonary artery in a manner similar to the treatment of the aortic cannula. This technique permits the four cannulas to lie close to each other without crossing, which is especially convenient in patients with small chest cavities. All four cannulas are brought out through the chest wall and across the skin below the costal margin, and connected to the Pierce-Donachy pump (Fig 5). These procedures were effected in 11 patients without extracorporeal circulation. In all patients the assistance was biventricular. The sternum has always been closed.

An infusion of heparin sodium is started when the bleeding from the chest drainage is less than 50 mL/h and the results of the coagulation tests show normal values. The dosage is adjusted to maintain an activated clotting time between 150 and 180 seconds.

Results

Of the 23 patients bridged, 20 underwent transplantation within a period ranging from 19 hours to 43 days. Three patients died on assistance because their condition could not be stabilized for the transplant procedure. The causes of death were uncontrolled bleeding in 2 patients and luxation of the left atrial cannula resulting in catastrophic bleeding in 1. In 9 patients, cardiac transplantation was performed within three days after implantation of the VAD; in 11, within eight days; and in the remaining 3, after 19, 31, and 43 days (Table 1). The 23 patients had a total of 165 days of assistance (mean support time, 7.1 days). Twelve patients were extubated during the period of assistance, and 18 were conscious.

Figures 6 and 7 show the mean hemodynamic variables before and after implantation. The mean cardiac index before implantation was 1.61 ± 0.25 L/min/m^2; at the moment of transplantation, it was 2.7 ± 0.27 L/min/m^2 for the left VAD and 2.1 ± 0.21 L/min/m^2 for the right VAD. These indexed flows permit the recovery from multiorgan failure.

None of the patients have sustained complications related to the device (electromechanical failure, infection, thromboembolism). Table 2 shows the complications not related to the device that were encountered in the 23 patients during the period of circulatory support. Bleeding was the most frequent complication and necessitated surgical exploration in 10 patients. The cause of bleeding was surgical in 5 of these patients, a coagulopathy in 1 patient, incorrect preclotting of the aortic cannula Dacron in 1, and surgical bleeding related to coagulopathy in 3.

In the group of patients having transplantation, 2 died of right ventricular failure due to pulmonary complications (fixed pulmonary hypertension and adult respiratory distress syndrome) on the second and third days after transplantation. Two patients died after 1 month, 1 of acute rejection and the other of a cerebral abscess. One patient died of graft insufficiency, 1 of hepatitis and pancreatitis, and 1 of chronic rejection one day, 29 days, and 60 days, respectively, after transplantation.

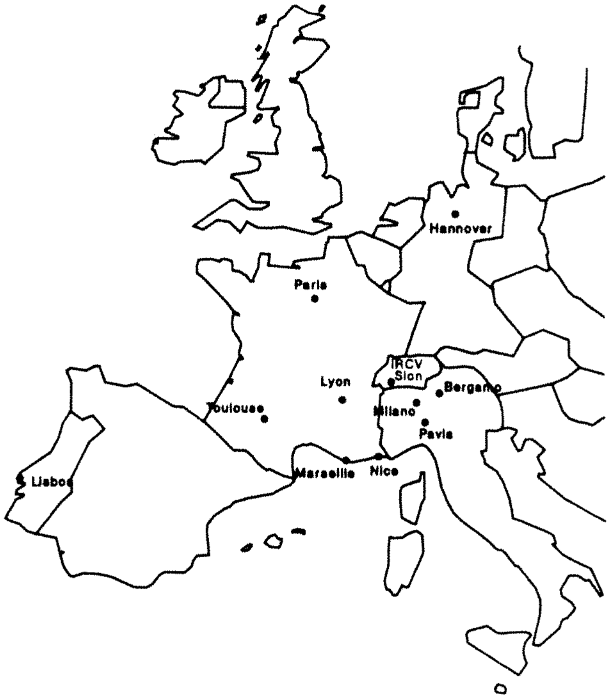


Fig 4. Bridge-to-transplantation team intervention centers in Europe.

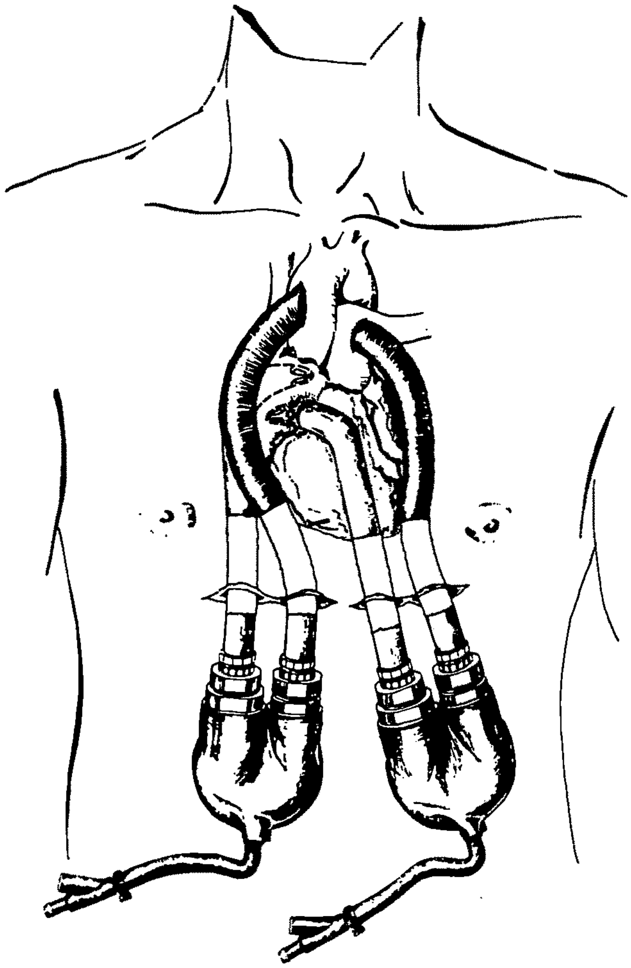


Fig 5. Surgical implantation of biventricular Pierce–Donachy pumps.

Comment

Contrary to the general expectation, the major complication of the procedure was not infection or thromboembolism but bleeding. This is the only really critical situation the BTT has been facing. Indeed, the major problem in the management of the patient on the VAD was bleeding. Therefore, the BTT does not recommend assistance or bridging to cardiac transplantation if the patient is seen with an important coagulopathy. For the same reason, we also prefer to implant the VAD without extracorporeal circulation. The anticoagulant therapy in these patients has to be evaluated in each patient based on the risk of hemorrhage. None of the patients showed clinical evidence of thromboembolism during assistance. Unlike the experience with orthotopic pumps, no infection episode, as already stated, was related to the external paracorporeal pumps.

In general, the BTT does not recommend transplantation before the patient has completely recovered from cerebral, pulmonary, renal, and hepatic problems. Our experience demonstrates that mortality (see Table 1) is not related to the length of the bridging period and that it is essential to let the patient recover completely from multiorgan failure before cardiac transplantation to assure a good chance of success for the operation. With the scarcity of donors, it is mandatory not to misuse a donor heart. In this respect, the BTT does not consider that the bridged patients should benefit from any priority over the established waiting list until they fully recover.

Table 1. Duration of Biventricular Assistance

Duration (days)	No. of Patients Bridged	No. of Patients Alive
≤3	9	4
3 to 8	11	7
>8	3	2

Concerning the paracorporeal position of the pumps, it has been observed that many patients find it less stressing to see the pumps outside the body. They believe that in that location, it would be easier to handle the situation in case of a major mechanical or electronic breakdown of the system.

For only 2 patients would the BTT maybe have chosen orthotopic pumps if they had been available in its standard equipment: the patient with the ventricular septal defect and the patient with tricuspid valve insufficiency. For the first patient, it has been possible to minimize the left-to-right shunt by increasing the emptying of the right atrium. For the second patient, the ventricular unloading allowed the valve annulus to recover a normal size and therefore to render the tricuspid valve competent again. Both patients, the first supported for 1 week and the second for 43 days, have received a transplant and are alive and well.

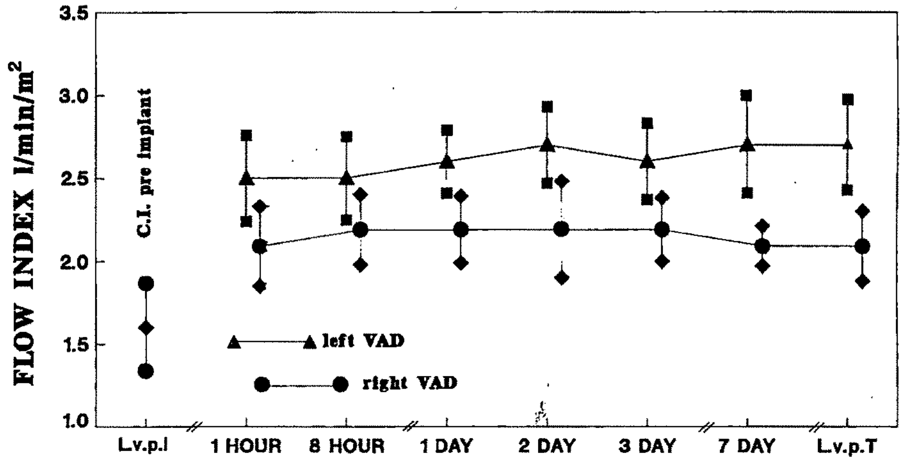
Conclusion

The SWAT team approach is generally thought useful by most medium to small transplantation centers, where a fully trained, constantly available team for less than 3 cases a year is financially not acceptable. Also, with so few cases, this team would probably lack experience. It is important that the calling center advise the BTT as soon as a critical situation appears and not wait until the situation gets out of hand. It is preferable for the BTT to be on standby even if its support will not be required than to be called in a high-emergency situation where the patient is

Table 2. Complications Not Related to Device

Complications	No. of Patients
Infection	4
Bleeding	11
Hemothorax	3
Pneumothorax	2
Lung contusion hemoptysis	1
Acute renal insufficiency	2
Luxation of left atrial cannula	2

Fig 6. Mean left and right cardiac indices (C.I.) for all patients on the ventricular assist devices (VADs) for more than seven days. (L.v.p.I. = last value prior to implantation; L.v.p.T. = last value prior to transplantation.)



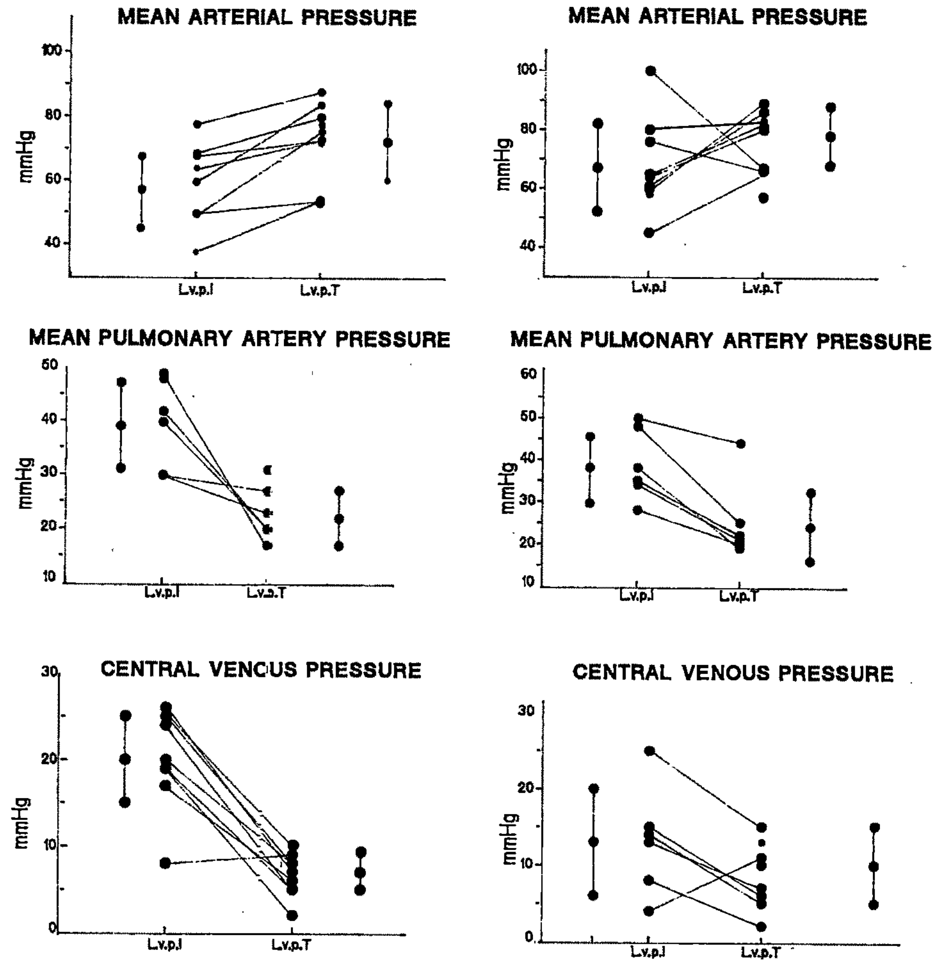
beyond the limits that can be handled by conventional drug and assistance therapy. Very few successes have been obtained in this critical situation, and the BTT consistently refuses cases in which, for example, the patient has undergone more than eight hours of circulatory support with conventional pumps (roller, centrifugal).

It is useful, if possible, for the BTT to visit the center where the operation is to take place, especially in Europe, where not only the plugs and fittings change from country to country but also the customs, formalities, and language. However, the success of the operation has never really been influenced by this previsit, as 9 bridging procedures have been done without it.

The main lessons we have learned from the use of this type of device are as follows:

Good patient selection and a good choice of the implantation time are mandatory for a successful procedure.

Fig 7. Mean pressures for all patients before the onset of ventricular assistance and before cardiac transplantation. Pressures shown on the left are for patients with idiopathic cardiomyopathy and those on the right are for patients with ischemic cardiomyopathy. (L.v.p.I. = last value prior to implantation; L.v.p.T. = last value prior to transplantation.).



The circulatory support provided by this type of pump permits the patient to recover from multiorgan failure.

The risks of thromboembolism and infection are limited.

Transplantation should be performed only when clinical recovery from multiorgan failure has taken place.

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General References

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Implantable Electrical Left Ventricular Assist System: Bridge to Transplantation and the Future

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An implantable left ventricular assist system (LVAS) utilizing an electromechanically driven dual pusher-plate blood pump has been employed in a multiinstitutional trial as a bridge to cardiac transplantation. Under development for permanent circulatory support in patients with end-stage heart disease, the LVAS, in this application, derives power and control from an external console via a percutaneous lead. The LVAS was implanted in 20 patients (16 men, 4 women) who were hemodynamically unstable or in refractory cardiogenic shock. The mean age was 44.9 years (range, 25 to 63 years). Preoperative diagnosis was evenly divided between end-stage ischemic disease, cardiomyopathy, and acute myocardial infarction. Implanted in the left upper quadrant within the anterior abdominal wall, the blood pump was connected between the left ventricular apex and ascending aorta. Total support of the systemic circulation and substantial left ventricular unloading were achieved with synchronous counterpulsation for periods up to 90 days (mean, 22.7 days). All patients were stabilized hemodynamically. The mean preoperative cardiac index of 1.5 L/min/m^2 increased by a factor of 2. Pulmonary arterial pressures decreased substantially. Serious complications occurred in 16 patients, precluding cardiac transplantation in 10. Most complications (>70%) were in patients who did not receive transplants; the most common complication was bleeding. Twelve of 13 patients with LVAS implants for more than seven days were mobilized, and 4 were fully ambulatory and completely rehabilitated. Orthotopic cardiac transplantation was performed in 10 patients after implants ranging from two to 90 days (mean, 30.3 days). Two patients died perioperatively, 1 of presumed sepsis and the other of donor-organ failure. Eight patients who received transplants were discharged and have been followed for 1 to 47 months (mean, 15.9 months). There have been no late deaths: 3 patients are working, 1 is a housewife, and all are in New York Heart Association functional class I. The bridging procedure provides an ideal setting for the initial clinical evaluation of, and offers an encouraging view of, the fully developed permanent LVAS.

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Over the two decades since the clinical success reported by DeBakey [1], considerable progress has been made in the application of pulsatile artificial ventricles to the treatment of profound myocardial failure refractory to conventional medical therapy and intraaortic balloon counterpulsation. Potentially reversible cardiac dysfunction has been managed with temporary circulatory support using left ventricular, right ventricular, and biventricular assist devices (VADs). Substantial myocardial salvage has been achieved in postcardiotomy [2, 3] and, less frequently, postinfarction [4] cardiogenic shock.

More recently, the focus of mechanical circulatory support has changed to the treatment of irreversible, terminal myocardial failure. Both "permanent" and temporary (staged) circulatory support have been employed using either auxiliary or replacement artificial ventricles. The permanent implantations performed by Kantrowitz and co-workers [5] in the early 1970s using an intraaortic LVAD (the dynamic aortic patch) were discontinued after severe infectious complications. Ten years later, a well-publicized experience in 5 patients with a permanent biventricular replacement device, or "artificial heart," was also discontinued after multiple complications including infection and thromboembolism [6, 7].

During the same period, building on the pioneering studies [8] and a decade of development by Shumway and colleagues, cardiac transplantation evolved from an experimental to a widely accepted therapeutic practice [9, 10]. It is the only currently available therapy for end-stage heart disease. The growth in cardiac transplantation, exponential in the first half of the 1980s, has slowed markedly in the last 2 years because of donor limitations [11]. More than 20% of the patients accepted for transplantation die while waiting for a suitable donor [12]. The majority of these potential recipients die, out of hospital, of fatal arrhythmias. However, many deteriorate hemo-

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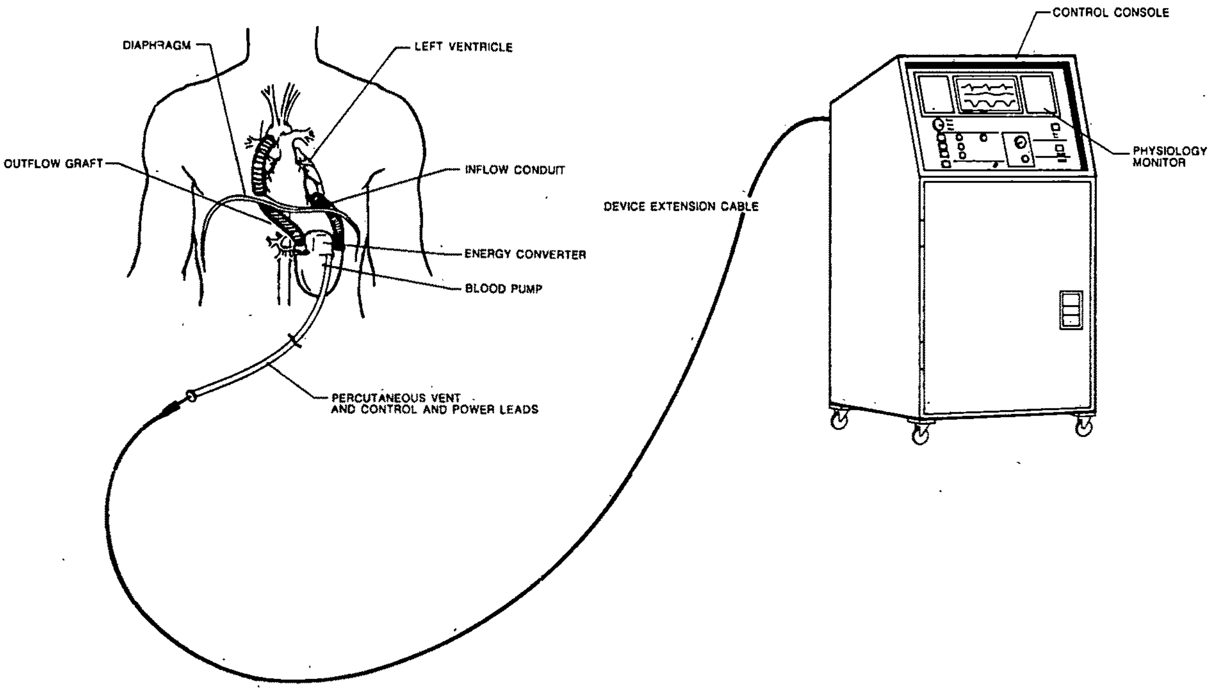

Fig 1. Configuration of Novacor left ventricular assist device illustrating implanted pump/drive unit and external control console.

dynamically and can be maintained with inotropic agents or mechanical circulatory support.

Temporary circulatory support as a bridge to cardiac transplantation was attempted by Cooley and colleagues [13] in 1969 with an orthotopic artificial heart in a patient who could not be weaned from cardiopulmonary bypass. Nine years later, Norman and associates [14] were among the first to use a VAD as a bridge, implanting an abdominal LVAD in a patient with ischemic myocardial contracture after double-valve replacement. Both of these patients died of infection within days of cardiac transplantation. Survival after transplantation following mechanical circulatory support was reported by Reemtsma and co-workers [15], who used the intraaortic balloon pump.

Successful bridging with a VAD was first accomplished by Portner and associates [16] in 1984 using the Novacor implantable electrical LVAD (Novacor Division, Baxter Healthcare Corporation, Oakland, Calif) in a patient with ischemic end-stage heart disease. Success with an orthotopic artificial heart was first achieved by Copeland and co-workers [17] a year later in a patient with viral cardiomyopathy. Since these successful procedures, and with a threefold increase in cardiac transplantation over the ensuing years accompanied by a growing shortage of donor organs, there has been an increasing use of assist [18–22] and replacement [21–24] devices in bridging procedures.

With one exception, all currently available pulsatile artificial ventricles are pneumatically actuated and inherently unsuitable for permanent circulatory support. The ventricles either are implanted and connected by percutaneous drivelines to an external drive unit or are paracorporeal with percutaneous access to the circulation. The electromechanically actuated Novacor device is part of a totally implantable left ventricular assist system designed for long-term circulatory support and now at an advanced stage of development [25]. This report details a multicenter experience in bridging to transplantation with the Novacor LVAD, and discusses implications for the future.

Material and Methods

Device Description

In its temporary configuration, the Novacor LVAD comprises two major components: an implanted pump/drive unit and an external control console (Fig 1). The pump/drive unit is positioned in the anterior abdominal wall of the left upper quadrant. It is connected to the console by power and control leads contained within a percutaneous vent tube. Traversing the diaphragm, externally reinforced low-porosity Dacron inflow and outflow conduits connect the pump between the left ventricular apex and the ascending aorta.

The blood pump consists of a seamless polyurethane sac bonded to dual, symmetrically opposed pusher plates and to a lightweight housing that incorporates valve fittings. The pump has a smooth blood-contacting surface and uses pericardial tissue valves with custom silicone flanges (Edwards CVS Division, Baxter Healthcare Corporation, Irvine, Calif). The pump geometry was designed for optimal flow patterns without areas of stasis, flow separation, or turbulence. Symmetrical sac deformation maintains the optimal flow throughout the pumping cycle. The dual pusher-plate blood pump is integrally coupled to an unique spring-decoupled pulsed-solenoid energy converter (Fig 2). Comprised of only two moving parts, this electromechanical drive provides efficient, durable, and reliable pump actuation. The integrated pump/

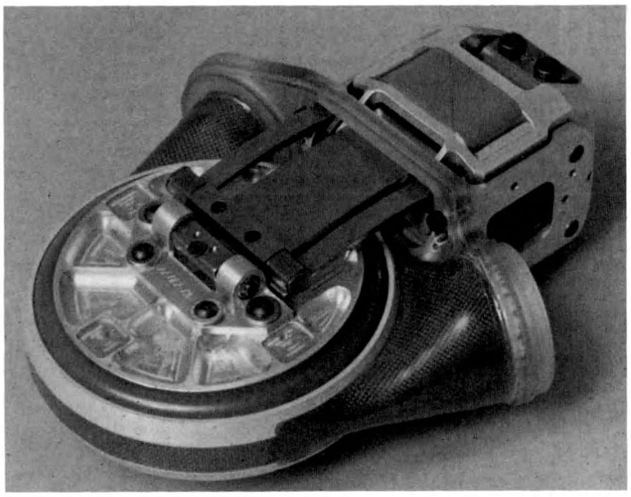

Fig 2. Pump/drive unit (unencapsulated) of the Novacor left ventricular assist device. Dual pusher-plate blood pump is closely integrated with the spring-decoupled solenoid energy converter.

drive unit is encapsulated by a fiberglass-reinforced polyester resin shell.

The control console provides electrical power and automatic control to the implanted pump/drive unit and continuously monitors critical patient and LVAD variables. The microprocessor-based controller and power circuitry are fully redundant, and uninterruptible power supplies enable patient transport and protect against power failure. A physiology monitor incorporated within the console simultaneously displays the patient's electrocardiogram, left ventricular and systemic pressure waveforms, and the pump volume trace. A cathode-ray tube terminal displays beat-by-beat digital information on device performance. Console panel controls and the terminal keyboard allow adjustment of operational variables and selection of control mode. Normal operation is synchronous counterpulsation based on internal sensors responsive to pump fill. Electrocardiogram-triggered synchronous and fixed-rate operation are also available.

The Novacor LVAD has a nominal maximum stroke volume of 70 mL and can pump in excess of 10 L/min. It is extremely responsive and can operate synchronously at cardiac rates as high as 240 beats per minute.

Protocols and Consents

After extensive preclinical evaluation and testing, clinical protocols and patient consent forms were reviewed and approved by each center's institutional review board and, subsequently, by the Food and Drug Administration (FDA). An investigational device exemption was granted by the FDA, and a clinical trial was initiated in September 1984 at Stanford University Medical Center. Supplemental approvals were obtained as the study expanded to additional centers.

Informed consent was obtained from the patient or the next of kin when all appropriate conventional therapy had been tried. No patient had known contraindications to cardiac transplantation. Multiorgan dysfunction, when present, was presumed to be secondary to low cardiac output and reversible with restoration of normal hemodynamics. Patients in whom contraindications developed after LVAD implantation were not considered for transplantation until the condition could be reversed, or were supported until they died.

Patient Selection

Since September 1984, the Novacor LVAD has been implanted as a bridge to cardiac transplantation in 20 patients (16 men and 4 women) ranging in age from 25 to 63 years (average age, 44.9 years). The preoperative diagnosis was end-stage ischemic disease in 6 patients, cardiomyopathy in 6 (3, idiopathic; 2, postpartum; 1, secondary to Adriamycin [doxoribicin hydrochloride] toxicity), acute myocardial infarction in 6, acute viral myocarditis in 1, and severe unresponsive rejection in 1 who had had previous transplantation (Table 1). One of these patients (patient 13) was bridged after unsuccessful revascularization and failure to be weaned from cardiopulmonary bypass.

Patient weight ranged from 55 to 91 kg (mean weight, 75.3 kg) and body surface area ranged from 1.67 to 2.19 m^2 (mean area, 1.94 m^2). Before LVAD insertion, all patients were in hemodynamically unstable condition or in cardiogenic shock on maximum pharmacological support, typically multiple inotropic agents and vasodilators and, frequently, antiarrhythmic agents. Thirteen patients had been supported by intraaortic balloon counterpulsation for periods ranging from a few hours to 30 days (average time, 7.0 days). The mean cardiac index before implantation, despite maximum conventional therapy, was 1.5 ± 0.6 L/min/m^2. The mean pulmonary artery pressure ranged from 22 to 49.5 mm Hg (average pressure, 34.5 mm Hg). Multiorgan dysfunction with severe renal and hepatic impairment was common. Two patients (patients 2 and 7) were oliguric and subsequently required hemodialysis. There were no significant differences in patient characteristics between those who ultimately had transplantation and those who did not.

Implantation Technique

The standard median sternotomy incision is extended to the umbilicus. A pocket is fashioned in the left upper quadrant between the costal margin and the iliac crest to accommodate the pump/drive unit. The plane of dissection is usually anterior to the posterior sheath of the rectus abdominis muscle. However, preperitoneal and subcutaneous placement were also used early in the series.

If the patient is in hemodynamically stable condition, the outflow graft is anastomosed to the ascending aorta before the institution of cardiopulmonary bypass. The graft is brought through the right hemidiaphragm anteriorly and connected to the blood pump. The heart is mobilized, and the left ventricular apex is encircled with pledgeted horizontal mattress sutures to secure the apical connector ring. The inflow conduit is connected to the pump, the pump is filled with saline solution, and the pump/drive unit is inserted into the previously prepared pocket. Using a special trocar, the percutaneous vent tube is tunneled inferiorly to the umbilicus to exit near the right anterior superior iliac spine. The vent tube is covered with

Table 1. Patient Characteristics and Outcome

Patient No.	Transplant Center	Age (yr)	Sex	Weight (kg)	Body Surface Area (m^2)	Diagnosis	Date of Implantation	Length of Implantation (days)	Outcome
1	Stanford University	51	M	81	2.02	IHD	09/05/84	8.5	Tx, alive (47 mo)
2	Stanford University	39	M	85	2.12	IHD	04/04/85	16	Died
3	St. Louis University	27	M	74	2.04	ACM	02/13/86	30	Died
4	Stanford University	47	M	65	1.82	AMI	06/05/86	4	Tx, alive (26 mo)
5	St. Louis University	46	M	88	2.10	IHD	09/10/86	90	Tx, alive (20 mo)
6	Stanford University	30	F	70	1.75	PCM	09/11/86	2	Tx, died (2 days)
7	Johns Hopkins	38	M	91	2.19	AMI	12/26/86	67	Died
8	Stanford University	42	M	82	2.12	IHD	01/23/87	7	Tx, alive (18 mo)
9	Stanford University	28	F	78	2.00	SR	02/13/87	<0.1	Died
10	Henry Ford Hospital	38	F	81	1.92	AVM	04/18/87	0.3	Died
11	University of Pittsburgh	55	M	80	2.07	ICM	07/03/87	0.4	Died
12	Henry Ford Hospital	43	M	74	1.93	ICM	08/14/87	5	Died
13	Vanderbilt University	47	M	75	1.88	AMI	09/27/87	33	Tx, died (2 h)
14	Vanderbilt University	56	M	77	1.94	AMI	11/14/87	5	Died
15	Stanford University	25	F	55	1.67	PCM	11/20/87	34	Tx, alive (7 mo)
16	St. Louis University	46	M	83	2.06	IHD	12/13/87	53	Tx, alive (6 mo)
17	Baylor College of Medicine	59	M	69	1.82	AMI	12/21/87	10	Died
18	University of Pittsburgh	63	M	72	1.93	IHD	03/22/88	23	Died
19	University of Pittsburgh	63	M	61	1.81	ICM	05/15/88	61	Tx, alive (1 mo)
20	University of Pittsburgh	55	M	69	1.67	AMI	05/28/88	10	Tx, alive (2 mo)

ACM = Adriamycin-induced cardiomyopathy; AMI = acute myocardial infarction; AVM = acute viral myocarditis; ICM = idiopathic cardiomyopathy; IHD = ischemic heart disease; PCM = postpartum cardiomyopathy; SR = severe rejection; Tx = transplantation.

Dacron velour for tissue fixation and with a long subcutaneous tunnel to reduce the potential for infection.

Cardiopulmonary bypass is then instituted, and the apical myocardium within the connector ring is excised. If present, mural thrombus is removed from the left ventricular chamber. The inflow conduit is then brought through the diaphragm, and the inflow cannula is secured within the connector ring. Residual air is evacuated from the pump, left ventricular chamber, and conduits through a needle vent.

Patient Management

Patients received minimal anticoagulation, typically intravenously administered low-dose heparin sodium or platelet-modifying drugs, or both. Four patients with the shortest implantation times (≤ two days) and 2 with severe bleeding complications received no anticoagulation. In 9 patients, low-dose heparin was administered, either alone (6 patients) or combined with low molecular weight dextran. Heparin, instituted when mediastinal drainage diminished, was titrated to maintain the partial thromboplastin time near 1.5 times normal. Two patients received only low molecular weight dextran. In 3 patients with extended LVAD support, low molecular weight dextran was replaced by orally administered warfarin sodium and dipyridamole (patients 9 and 16) or dipyridamole and aspirin (patient 15).

All patients received prophylactic antibiotics (typically a broad spectrum cephalosporin) in the perioperative period. Subsequently, antibiotics were administered only for documented infection.

Pharmacological support was required in some patients for concomitant transient right heart failure. Inotropic drugs included isoproterenol hydrochloride and dopamine hydrochloride. Some patients received pulmonary vasodilators, usually sodium nitroprusside and nitroglycerine but occasionally prostaglandin E_1 (patients 2 and 14). A centrifugal RVAD was placed in 3 patients (patients 10, 11, and 17).

Hemodynamic monitoring in the early postoperative period typically included central venous, pulmonary artery, and radial artery pressures as well as cardiac output. A sensor-tipped catheter (Millar Instruments, Houston, Tex) was routinely placed for left ventricular pressure to provide a measure of LVAD performance and phasing. Pump stroke volume and output were continuously available from the Novacor console.

Device Explantation and Cardiac Transplantation

After cardiopulmonary bypass is established, the pump inflow and outflow conduits are cross-clamped, transected, and freed from adhesions. The percutaneous vent tube is transected, and the exposed ends are covered with povidone-iodine–filled silicone caps to prevent contamination. The pump/drive unit is removed from the surgical field, and the vent tube is withdrawn from the subcutaneous tunnel.

Orthotopic cardiac transplantation is then carried out in the normal manner [8]. The standard immunosuppression protocol, usually triple-drug therapy of cyclosporine, azathioprine, and prednisone, is not modified for bridged patients.

Results

The duration of LVAD implantation in this series of 20 patients ranged from one hour to 90 days (average duration, 22.7 days) (see Table 1). Ten patients underwent transplantation after having had the implant from two to 90 days (average time, 30.3 days), with extended support in 5 (90, 33, 34, 53, and 61 days). Of the other 10 patients who died of complications, only 1 (patient 7) was a suitable transplant candidate at the time of death.

Hemodynamic Function

All patients were stabilized hemodynamically (if only transiently in some). The mean cardiac index increased significantly ($p < 0.005$) from 1.5 ± 0.6 (before implantation) to 3.2 ± 0.4 $L/min/m^2$ (average during LVAD support) in the patients having transplantation, and from 1.5 ± 0.4 to 3.0 ± 0.8 $L/min/m^2$ in those not having transplantation (Fig 3). Substantial left ventricular unloading was achieved in all patients. Peak left ventricular pressures remained consistently lower than systemic pressures with pump capture of the entire cardiac output. Pump flows ranged from 3.3 to 8.2 L/min. In both groups of patients, mean values increased significantly ($p < 0.005$) for mean arterial pressure and decreased significantly for mean pulmonary artery pressure with LVAD support (see Fig 3). Although the hemodynamic effects were somewhat more pronounced in the patients ultimately having transplantation, the differences between the two groups were not significant.

Vital Organ Function

Normal or significantly improved renal function (mean: creatinine, 1.2 mg/dL; blood urea nitrogen, 27.4 mg/dL) resulted from the increased cardiac output during circulatory support in the patients receiving a transplant. Renal function was substantially worse (mean: creatinine, 4.1 mg/dL; blood urea nitrogen, 78.0 mg/dL) in those not having transplantation. Similar improvements were documented for the transplant group in hepatic and pulmonary function.

Hematological Variables

Excluding the patients with severe bleeding diatheses, hematological variables were within normal limits. Hemolysis was not clinically significant, with plasma hemoglobin levels typically well below 5 mg/dL. After a transient reduction during the immediate postoperative period, platelet counts remained within the normal range. Normal platelet function, without evidence of activation, was documented after 3 months of LVAD support [26].

Complications

Serious complications occurred in 16 patients and precluded cardiac transplantation in 10 (Table 2). The majority (>70%) were in patients who did not undergo transplantation. There were two or more complications in 8 patients, only 1 of whom (patient 5) underwent transplantation. The most common complication was bleeding; it occurred in 8 patients (40%) and necessitated reoperation in 4. Hemorrhage and coagulopathy were major contributing causes in the deaths of 4 patients (patients 7, 9, 11, and 18).

Six patients had documented infections during the period of device implantation. An additional patient had intermittent febrile episodes with an elevated white blood cell count but no positive cultures. The main infectious organisms were *Candida albicans*, *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Pseudomonas*, and *Enterobacter*. Infection (bilateral fungous pneumonia) was the primary cause of death in 1 patient (patient 2). Two patients who underwent transplantation had infections involving the implanted device: 1 (patient 5) had an *S epidermidis* infection of the percutaneous vent tube attributed to a short tunnel and inadequate fixation, and the other patient (patient 16) had an *S aureus* infection of the device pocket, probably secondary to prolonged placement of a drainage tube.

Severe right heart failure occurred in 5 patients. A centrifugal RVAD was used in 3 patients (patients 10, 11, and 17) and vasodilation with prostaglandin E_1 was used in 2 (patients 2 and 14). Admitted with severe congestive heart failure and pulmonary edema secondary to acute viral myocarditis, 1 patient (patient 10) died of respiratory failure despite biventricular circulatory support. Before LVAD implantation, another patient (patient 14) sustained a massive myocardial infarction with major involvement of the right ventricle; volume loading, inotropic support, and vasodilation were minimally effective.

Renal failure was a contributing cause of death in 4 patients (patients 2, 3, 7, and 14). Two patients (patients 3 and 14) died of multiorgan failure. One patient (patient 7), anuric before LVAD implantation because of prolonged hypotension during cardiac arrest, required hemodialysis for an extended period but recovered near-normal renal function. Accidental hemorrhage and disseminated intravascular coagulopathy were the primary causes of death.

Two patients sustained perioperative fatal cerebrovascular accidents, 1 (patient 12) from the embolization of a left ventricular mural thrombus (seen preoperatively on echocardiogram) and the other (patient 17) from an air embolus secondary to a deairing complication. One patient (patient 19) experienced two transient focal neurological events, probably of embolic origin, the first resulting in expressive aphasia and the second in left hemiparesis. At device explantation, an unusual fibrin deposition was noted on the distal stents of the pump inflow valve and was attributed to a number of potentially predisposing factors. The patient was minimally anticoagulated and had atypically low pump flows in a setting of abnormal blood rheology (high viscosity) and an extremely high circulating fibrinogen level.

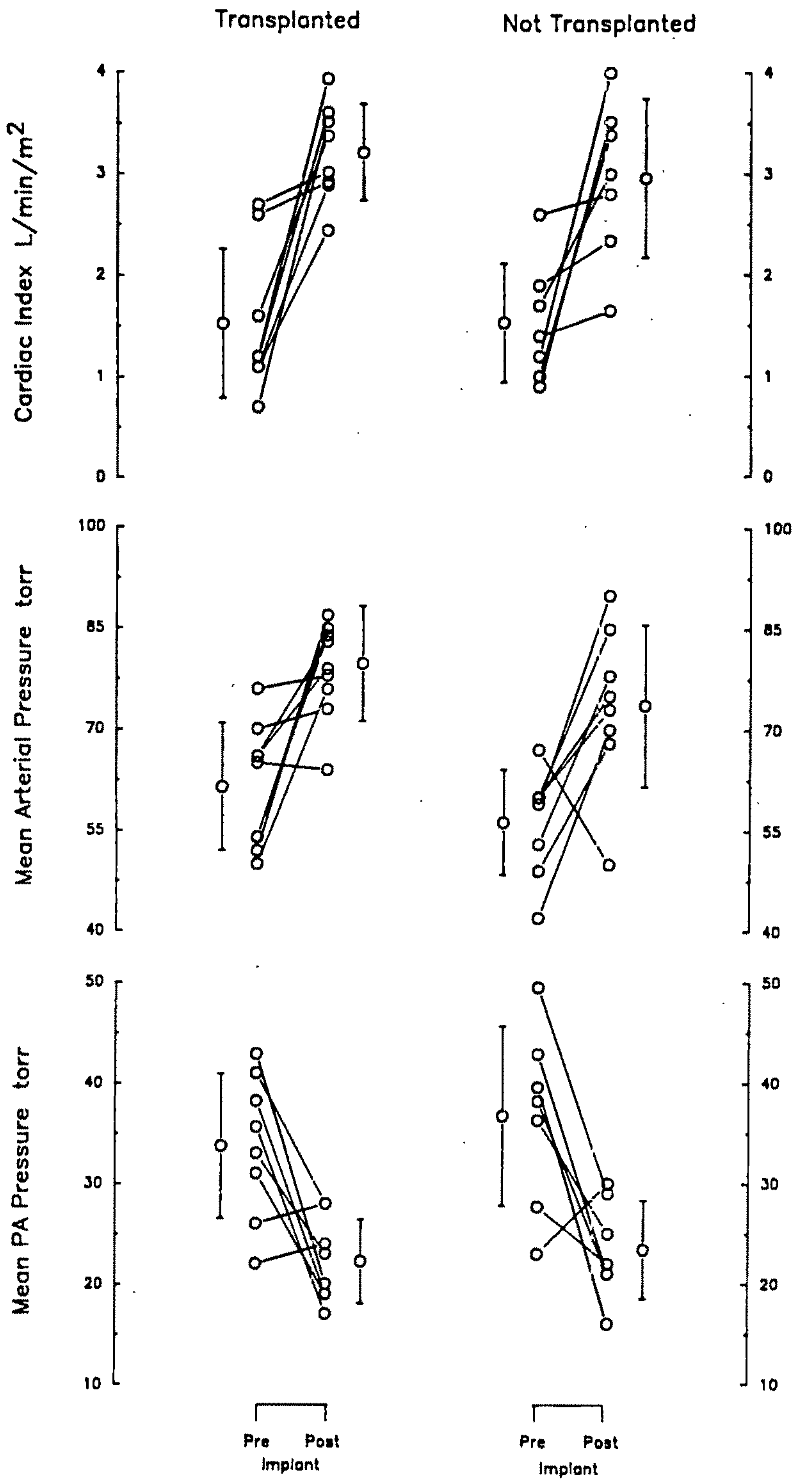

Fig 3. Hemodynamic function before (Pre-Implant) *and during* (Post-Implant) *left ventricular assist device support for bridged patients who did and did not undergo transplantation. Mean postimplant values for all variables were significantly* ($p < 0.005$) *different from preimplant values.* (PA = *pulmonary artery.*)

A patent foramen ovale was closed at the time of LVAD implantation in 2 patients. Initially unrecognized in a third patient (patient 13), the reduced left atrial pressure with synchronous assist pumping resulted in a substantial right-to-left shunt and hypoxia. Confirmed by microbubble echocardiogram, the shunt resolved in a few days.

High levels of antibodies were present in 2 patients, presumably secondary to multiple transfusions of blood products [20]. Antibodies to platelets developed in 1 patient (patient 3) and resulted in an increased need for platelet transfusions. A high level of cytotoxic antibodies developed in another patient (patient 5), but the level declined from 87% to 7% over 10 weeks of LVAD support, thereby facilitating negative crossmatch to potential donors and eventual cardiac transplantation.

One patient (patient 2) had persistent ventricular tachycardia unresponsive to a battery of antiarrhythmic drugs. However, normal systemic pressures and a reasonable

Table 2. Complications During Left Ventricular Assist Device Support

Complication	No. Having Transplantation	No. Without Transplantation
Bleeding	3	5
Infection	3	4
Right ventricular failure	0	5
Renal failure	0	4
Neurological	1	2
Patent foramen ovale	1	2
Antibodies	1	1
Arrhythmia	0	1

cardiac index were maintained with synchronous LVAD operation at rates as high as 200 beats per minute.

In more than 15 months of cumulative operation, there were no malfunctions or device-related complications.

Clinical Outcome

Of 13 LVAD–bridged patients supported for a week or longer, only 1 (patient 2) could not be mobilized out of bed. Four patients who had had the implants for longer than 1 month were fully ambulatory, walking more than a kilometer each day with assistance in moving the console. Several patients also exercised on a stationary bicycle. Pump output automatically increased by as much as 50% with exercise. Of the 10 patients receiving orthotopic cardiac transplants, 5 had complications in the early posttransplantation period. One patient (patient 1) sustained a colon perforation 2 weeks after transplantation and required a temporary diverting colostomy. Six weeks later acute cholecystitis developed, necessitating cholecystectomy. Neither complication was associated with device placement, and both completely resolved. Two patients with infections, one of the pump/drive unit pocket and the other of the vent tube subcutaneous tract, responded to debridement and topical parenteral antibiotics. One patient (patient 6) died two days after transplantation of profound peripheral vasodilatation and multiorgan failure. Sepsis was presumed, but no organism was isolated. Another patient (patient 13) died perioperatively of graft failure.

Eight cardiac allograft recipients were discharged and have been followed 1 to 47 months (average time, 15.9 months) after cardiac transplantation. There have been no late deaths. Three recipients are working, 1 is a housewife, and all are in New York Heart Association functional class I.

Comment

The results of this clinical trial demonstrate that bridging to cardiac transplantation with the implantable Novacor LVAD can be successfully accomplished without undue mortality or morbidity. A series of 20 patients with refractory terminal heart failure were stabilized hemodynamically with markedly improved end-organ perfusion. In half, severe multiorgan dysfunction resolved, and orthotopic cardiac transplantation was achieved after two to 90 days of synchronous circulatory support. Hematological variables were within normal limits over extended periods, with normal platelet function and no clinically significant hemolysis over extended periods.

As in other recently reported series [18–24], these morbidly ill patients were characterized by multiple complications. Bleeding and infection were the most common (45%). Bleeding was the major contributing cause of death in nearly half (40%) of the patients not undergoing transplantation. Thromboembolism, a major risk with all intravascular devices, occurred in only 1, apparently predisposed, patient without long-term neurological deficit. The optimal level of anticoagulation and the optimal combination of anticoagulant and platelet-antiaggregating agents are not yet known.

Infectious complications in this series were predominantly associated with longer-term implants, but were not strictly device related. Two surviving transplant patients had infections involving the implanted device, both procedure related. One patient, not undergoing transplantation, died of fungal pneumonia secondary to prolonged endotracheal intubation, and another died of presumed sepsis within two days of transplantation. This incidence of fatal infection is considerably less than that reported for the orthotopically implanted artificial heart, both as a bridge [27] and as a "permanent" implant [28]. Mediastinal infection was the primary cause of death in 40% of artificial heart–bridged patients and in all patients with a permanent artificial heart. Accumulation of clotted blood and serum in dead spaces and the avascular nature of the prosthetic ventricles were thought to limit local host defenses against hematogenous infection. Over a longer term, the pulsatile, percutaneous air drivelines inevitably provide a portal of entry for infection.

Other complications in the current series were largely a consequence of patient selection and timing, which in the end were the most important determinants of overall survival. Patients with contraindications to cardiac transplantation were not knowingly accepted for bridging. Renal, hepatic, and pulmonary dysfunction, when present, were presumed to be reversible. Renal failure is considered by some investigators [29] to be an absolute contraindication to the bridging procedure. However, 1 patient in the current series, anuric at the time of implantation, recovered near-normal renal function after 2 months of dialysis and LVAD–increased cardiac output. The importance of a patent foramen ovale in left ventricular assist pumping has been described previously [30]. Relatively common, a patent foramen ovale can be a lethal complication in this setting, with severe right-to-left shunting and hypoxia. It warrants routine careful inspection and closure.

An inherent limitation of isolated LVAD support is found in the patient with severe right heart failure, pulmonary hypertension, and a high, fixed pulmonary vascular resistance. However, such a patient does not represent a suitable candidate for orthotopic cardiac transplantation and is, therefore, also contraindicated for the bridging procedure. The LVAD function (with left ventricular cannulation) decompresses the left ventricle, significantly reducing left atrial pressure. In a patient with normal (or near-normal) pulmonary vascular resistance, this results in a substantial reduction in right ventricular afterload or pulmonary artery pressure. This is illustrated in Figure 3, which documents decreases of up to 60% in the mean pulmonary artery pressure for the current series of bridged patients. The LVAD operation, therefore, indirectly provides simultaneous circulatory support of the right ventricle.

Severe right heart failure, refractory to LVAD or inotropic support, is often due to pulmonary vasospasm and is responsive to prostaglandin E_1 [19]. In the current study, 2 patients were treated with prostaglandin E_1 but died of other complications. Three patients were placed, without success, on concomitant RVAD support. Some of the patients who had transplantation required transient pharmacological support of the right ventricle. Many patients with apparently severe biventricular failure have demonstrated an immediate and significant response to univentricular (LVAD) support. It is not entirely clear, therefore, why so many patients in other programs are now bridged with biventricular support. The risks associated with the use of two pumps (and four valves) must be greater than with a single pump.

Since the first clinical success in 1984 [16], the worldwide annual number of bridge-to-transplantation procedures has increased from a handful to approximately 100. Over the same period, there has been a fourfold increase in cardiac transplantations in the United States and a threefold increase worldwide [11]. In 1987, the number of transplantation centers increased 40% in the United States and 65% worldwide. However, growth in the number of transplantations, now limited by donor availability, slowed to 15% and the donor waiting period increased substantially.

With the growing shortage of donor organs and the expanding indications for cardiac transplantation, there is an increasing need for a mechanical alternative. The most useful permanent heart substitute will be the totally implantable, electrically powered left ventricular assist system [31]. Under development for 18 years in the artificial heart program of the National Heart, Lung, and Blood Institute, the implantable Novacor left ventricular assist system is now approaching clinical use [32]. An implanted electronic controller with rechargeable batteries replaces the current control console, and power is transmitted, from an externally worn battery pack, across the intact skin by inductive coupling. Two-year system-reliability testing under refereed test conditions is at an advanced stage as part of a preclinical device-readiness testing program [33]. Twelve complete systems have been under test, continuously without failure, for an average of 15 months, with nine exceeding 1 year and three exceeding 18 months. Studies in experimental animals, initially of components and subsequently of integrated systems, have been underway since 1972. Implantations of progressively longer duration have been achieved, with more than 20 exceeding 3 months and the longest extending to 9 months.

The temporary configuration of the Novacor LVAD has been used in a series of 20 patients bridged to transplantation. Ten patients underwent transplantation after LVAD support for periods ranging from two to 90 days. Patients were fully ambulatory and rehabilitated by the implanted system; end-organ function was restored. There were no device-related complications. Eight patients were discharged from the hospital and have been followed for 1 to 47 months after transplantation. There have been no late deaths, a finding indicating survival comparable with conventional cardiac transplantation.

In addition to providing a therapeutic option for select patients with terminal heart failure, the bridge-to-transplantation procedure offers a unique opportunity to evaluate LVAD function and patient response. The transplant recipient represents the ultimate candidate for permanent mechanical circulatory support. As permanent left ventricular assist system development and preclinical testing near conclusion, the reported initial clinical experience provides an encouraging view of the future potential of the fully integrated, implantable permanent system.

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Total Artificial Heart: Survival and Complications

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A total artificial heart was implanted in 28 patients as a bridge to transplantation. Mean time of mechanical support was 14.8 ± 10 days. The 70-mL Jarvik-7 was used in 12 patients and the 100-mL Jarvik-7 in the remaining 16. No clinical thromboembolic complications occurred during implantation. There was no postoperative bleeding requiring operation. Both survival and the rate of complications were similar in the two Jarvik-7 groups. Eleven patients underwent successful transplantation, and 1 patient is still on mechanical support. Sepsis and multiple-organ failure were the most important causes of death. All patients receiving the total artificial heart for severe acute rejection after transplantation died of infection. Early implantation of the total artificial heart is advised in younger patients and in older patients with acute cardiac failure. The use of this device should be contraindicated in immunosuppressed patients because of the high risk of infection.

(Ann Thorac Surg 1989;47:151–7)

More than 30 years have passed since Akutsu and Kolff [1] in 1957 obtained survival of an animal after the implantation of a total artificial heart (TAH). Twelve years later, in 1969, Cooley and associates [2] attempted clinical use of the TAH as a bridge to transplantation. Sixteen more years of improvements in design, biomaterials, and technologies permitted the successful use of a Jarvik-7 TAH as a bridge to transplantation in 1985 [3].

The TAH program began at La Pitié in 1985, and since April 1986, 28 implantations have been carried out. We present here the results to date with the Jarvik-7 artificial heart.

Material and Methods

Diagnoses and Indications for Implantation

The recipients included 24 men and 4 women with a mean age of 40.4 ± 12 years (range, 19 to 56 years). The causes of heart disease are summarized in Table 1. The most common indication for TAH implantation was ischemic heart disease followed by idiopathic cardiomyopathy. Four patients received a TAH because of severe acute rejection. Two patients had a postpartum cardiomyopathy, and 1 patient had a terminal valvular disease. The most recent patient seen has an idiopathic cardiomyopathy and is still receiving support from the TAH. This patient is in good condition. In 3 patients, cardiopulmonary bypass was prolonged because they could not be weaned in a previous operation.

The indication for implantation of the TAH was a desperately ill patient with an expected survival of less than 48 hours or signs of rapid hemodynamic deterioration, or both. The TAH was used after the failure of all conventional modes of therapy when there were no contraindications to transplantation.

Preoperative Status

Renal function was mildly deteriorated in 10 patients (35.7%) and markedly deteriorated in 6 (21.4%) as a result of a low cardiac output state. One patient required preoperative dialysis.

Nine patients (32.1%) were in severe pulmonary edema. Mild or marked hepatic insufficiency and coagulation abnormalities were found in all patients.

Two patients were in cardiac arrest when they were taken to the operating room.

Surgical Technique

A complete description of the operative procedure has been previously published [4].

To diminish cardiopulmonary bypass time, the drivelines were positioned and the artificial ventricles tested systematically before extracorporeal circulation.

All implantations were carried out under cardiopulmonary bypass and general hypothermia (27° to 28°C). After the division of the great vessels just above the aortic and pulmonary valves and after the excision of the natural ventricles with 1 cm of the ventricular wall left in place, the atrial cuffs were prepared and sutured. This was followed by the placement of the aortic and pulmonary connectors. Gelatine Resorcine Formol Glue was used in all operations to assure hemostasis (Fig 1). After the connection of the left and right artificial ventricles (Fig 2), the activating procedure was started, both ventricles were purged, and cardiopulmonary bypass was gently decreased while the function of the TAH was increased. All the devices were implanted in the medial position (Fig 3), and efforts were made to avoid any compression of the venous return and the left lung. Sternal closure was carried out with continuous monitoring of the hemodynamic variables to detect early malposition of the artificial heart. The patients were monitored in the operating room

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Table 1. Causes of Heart Disease and Extent of Decompensation

	Decompensation	
Cause	Acute	Chronic
Ischemic heart disease	6	5
Idiopathic cardiomyopathy	4	5
Rejection after transplantation	0	4
Postpartum cardiomyopathy	2	0
Valvular disease	0	1
Still under TAH support	0	1
Total	12	16

TAH = total artificial heart.

for two to four hours to assure hemostasis and adequate hemodynamic function.

Total Artificial Heart Control

We tried to obtain a cardiac output of 100 mL × weight (kilograms), with an ideal filling volume at 70% to 80% of full capacity so that both ventricles could operate in the steep portion of the Starling curve. The frequency was calculated by dividing the ideal calculated cardiac output by the filling volume. We tried to keep left atrial pressure lower than 15 mm Hg to avoid pulmonary edema, and we also tried to keep right atrial pressure as low as possible to avoid the decrease in the glomerular filtration rate caused by renal venous hypertension.

Coagulation Control

Coagulation was checked preoperatively by studying the status of the platelets, and the coagulation and fibrinolytic systems. The coagulation protocol is summarized in the following list. Modifications may be necessary during implantation.

Prothrombin time
Activated partial thromboplastin time
Reptilase time
Fibrinogen titration
Recalcified whole blood thromboelastography
Platelet aggregation to adenosine diphosphate, epinephrine, collagen, and arachidonic acid by Born method
Plasma and serum antithrombin III (AT III) titration. Estimate of antithrombin potential index (API): API = plasma AT III − serum AT III
Plasma and serum factor X titration
Hematocrit
Platelet count
Platelet aggregate evaluation by Wu–Haok method
Ivy–Borchgrevink bleeding time
Fibrinopeptide A
Fibrinogen degradation products
α-2-antiplasmin
Platelet factor 4
β-Thromboglobulin
Raby's transference test in thromboelastography

The anticoagulation regimen used during TAH implantation was as follows:

Heparin sodium, 1,000–5,000 IU/day
Dipyridamole, 150–300 mg/6 h
Aspirin, 50 mg/day
Aprotinin, 1,000,000 PI/U/IV + 4,000 PI/U/min
Pentoxyphylline, 400 mg/d
Ticlopidine, 250 mg/2–3 d
Fresh plasma, antithrombin III, blood cell concentrates according to the evolution of the patient's state

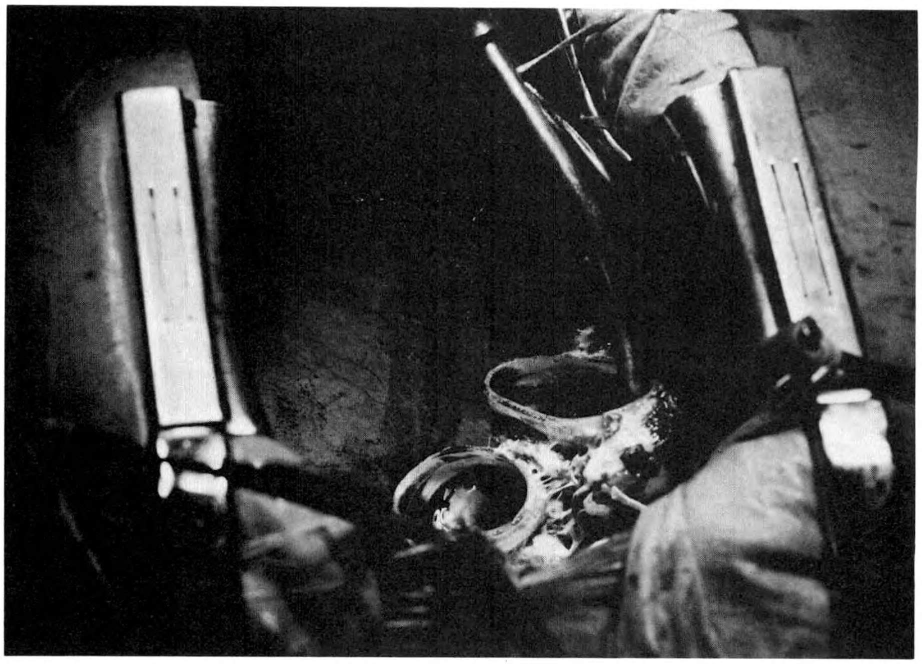


Fig 1. Intraoperative view of the two atrial cuffs after the use of Gelatine Resorcine Formol Glue.

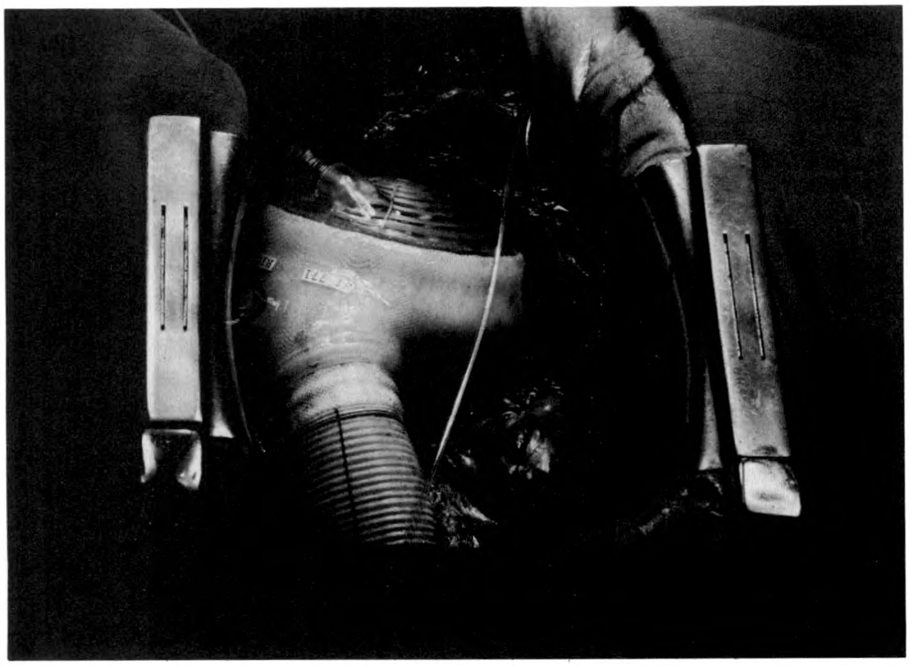


Fig 2. Intraoperative view of the total artificial heart in the medial position. Note the left atrial and pulmonary artery pressure catheters.

Results

Clinical Course

The clinical results in our 28 patients are summarized in Figure 4. The response was considered favorable when the patient met all the criteria for transplantation. The mean age of the overall group was 40.4 ± 12 years. The mean time of mechanical support was 14.8 ± 10 days (range, two to 42 days). Twelve patients received a 70-mL Jarvik-7 heart and 16, a 100-mL Jarvik-7 heart. No significant differences were found in survival and the rate of complications between the two Jarvik-7 groups. Major intraoperative complications were a tear in the quick connection between the atrial cuff and the ventricle that required replacement of the cuff and two cases of abnormal function of the diaphragm at the preimplantation test, which made it necessary to change the ventricles. A mismatch between the TAH and the thorax occurred in 1 patient and made sternal closure impossible. There were no cases of postoperative bleeding requiring operation, and there was no clinical evidence of thromboembolic complications. Hemolysis was at a clinically insignificant level during all the implantations.

Results of Mechanical Support

The influence of age on the outcome is shown in Figure 5A. Patients older than 40 years had a mortality of 83% with TAH support, more than four times higher than the mortality in the younger group (18%). Long-term survival is also different between these two groups; 8% in patients older than 40 years and 54.5% in younger patients.

The influence of the evolution of the disease on the outcome is summarized in Figure 5B. The combined influence of age and evolution of the disease is presented in Figure 6. In the chronic decompensation group (see Fig 6A), 100% of the patients older than 40 years died during mechanical support compared with 17% of the patients younger than 40 years. Eighty-three percent of the younger group had transplantation, and long-term survival is 50%.

In the acute decompensation group (see Fig 6B), only 29% of the patients older than 40 years underwent transplantation compared with 80% of the younger group. Long-term survival was 14% in the older group and 60% in the younger group.

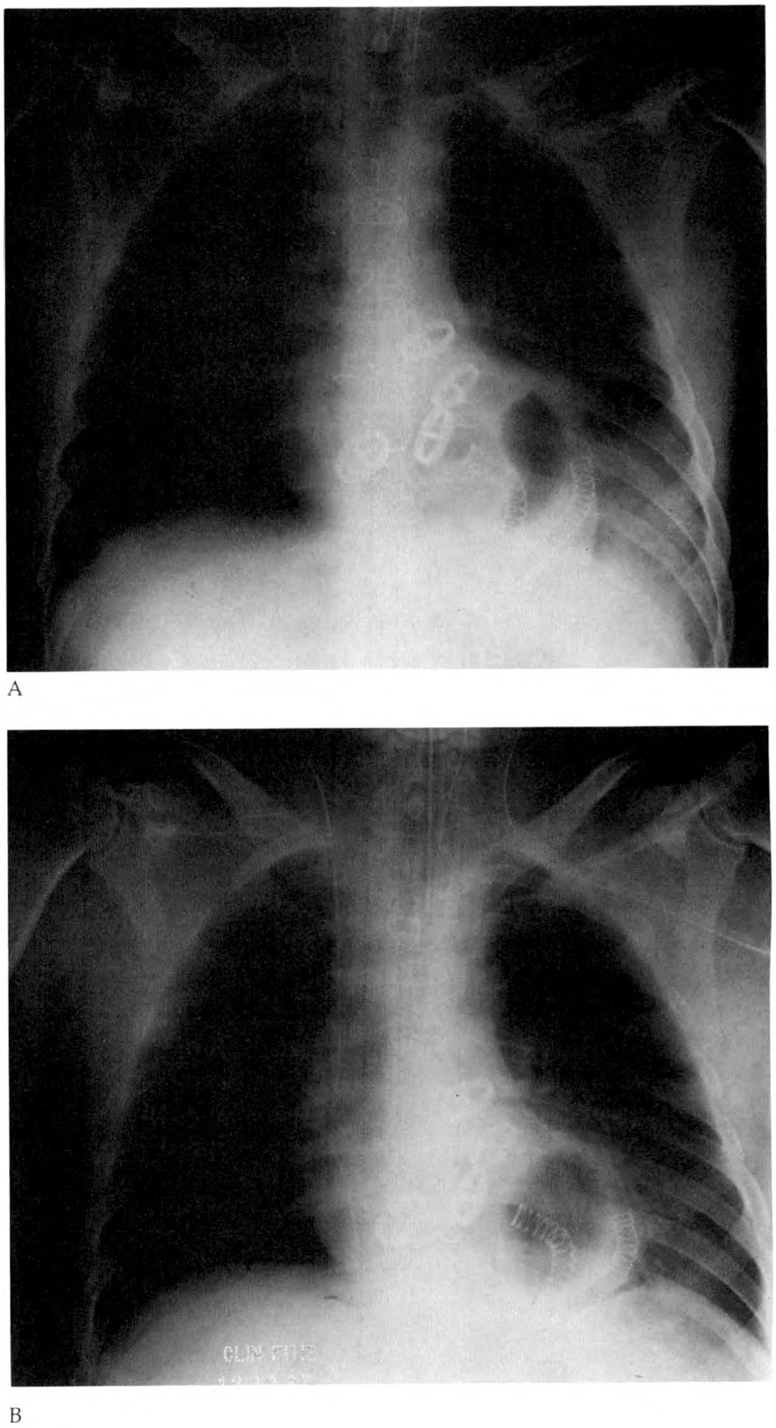
The indices of renal function before and during TAH support were examined in 24 patients. The mean preoperative blood urea nitrogen (BUN) level was 21 mmol (range, 9 to 58 mmol), and the mean maximum postoperative level was 28.8 mmol (range, 12 to 90 mmol). After seven days of mechanical support, the mean value (16 patients) decreased to 15.1 mmol. The mean preoperative creatinine level was 284 μmol (range, 78 to 476 μmol) and the mean maximum postoperative value was 330 μmol (range, 100 to 775 μmol). The creatinine level also decreased after seven days of TAH support (mean value, 148 μmol). Four patients (14.3%) required postoperative dialysis.

The TAH was implanted in 4 patients (14.3%) because of severe rejection after transplantation. All of these patients died during mechanical support.

Overall mortality during TAH support was 57.1% (16 patients) (see Fig 4). The main causes of death were sepsis (8 patients, 28.6%) and multiple-organ failure (5 patients, 17.9%). Two patients (7.1%) died of both of these causes. One patient died of pulmonary embolism originating from phlebitis at the pelvic level.

The origin of the infection in the 10 patients who died of sepsis was detected in 7. The lung was the origin in 4. The driveline, the urinary tract, and purulent peritonitis were the sources in the other 3 patients.

Fig 3. Chest roentgenograms demonstrating medial placement of the 100-mL Jarvik-7 total artificial heart (TAH). (A) Note TAH in middiastolic phase as evidenced by the air in the left artificial ventricle. (B) The TAH in end-systolic phase.



The mean follow-up of the 11 patients having transplantation is 295 days; the total number of days after transplantation is 3,253. In the immediate posttransplantation period, an infection developed in 5 of these patients. Three were adequately treated with antibiotics; 2 died. Two other patients died during follow-up of causes not related to the TAH: 1 of anoxic coma and the other of a multicentric Kaposi sarcoma secondary to immunosuppression treatment (azathioprine).

Comment

Since 1969 when Cooley and co-workers [2] described the use of the TAH as an interim device, several improvements in pneumatic TAH technology and biomaterials have occurred. In the last decade, many institutions started research programs in mechanical circulatory support and developed several types of device [5–7]. At present, more than 80 implantations around the world

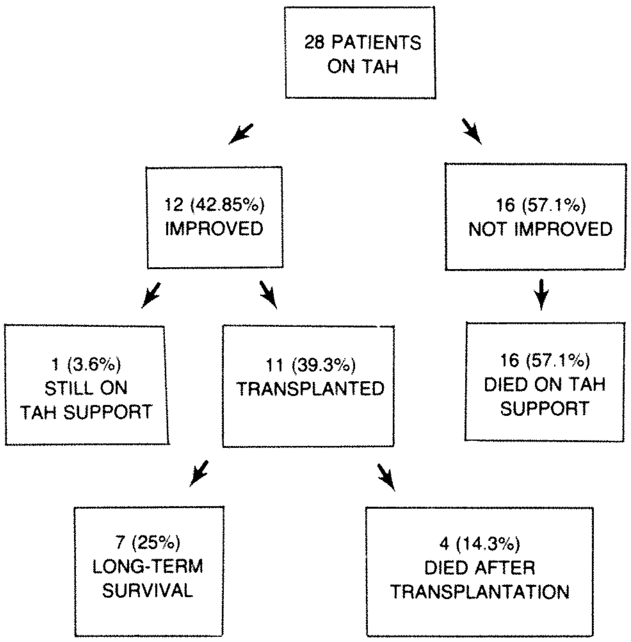

28 PATIENTS ON TAH
12 (42.85%) IMPROVED
16 (57.1%) NOT IMPROVED
1 (3.6%) STILL ON TAH SUPPORT
11 (39.3%) TRANSPLANTED
16 (57.1%) DIED ON TAH SUPPORT
7 (25%) LONG-TERM SURVIVAL
4 (14.3%) DIED AFTER TRANSPLANTATION

Fig 4. Clinical results in 28 patients. (TAH = *total artificial heart.*)

demonstrate the clinical usefulness of mechanical bridge procedures [8].

Our experience with the Jarvik-7 TAH comprises 28 patients. Eleven (39.3%) of these patients had a successful transplantation, and 7 (25%) are at home in excellent condition. Sixteen patients (57.1%) died under mechanical support. Infection was the major cause of death in our series. Seven patients (25%) died of sepsis and 3 (10.7%) died of a combination of sepsis and multiple-organ failure. Four patients (14%) received a TAH because of severe acute rejection after transplantation. All these patients died of infections when they were on mechanical support. We believe that the immunological status of the patients who had a transplant, a status aggravated by a previous medical approach to treatment of severe acute rejection, strongly increased the risk of infection; in the future, previous transplant could be considered a contraindication to use of the TAH.

Three patients received a TAH because they could not be weaned from cardiopulmonary bypass after operation. Two of them required a TAH because of an intraoperative transplant failure. A previous attempt at mechanical right ventricular assistance was carried out and failed in 1 patient. In that same patient, an improper evaluation of patient size caused a mismatch between the TAH and thorax, thereby making sternal closure impossible. The duration of extracorporeal circulation was an important determinant in the development of multiple-organ failure, which was the cause of death in both patients who received a TAH after a failed transplantation.

Renal function prior to implantation was critical in many of our recipients. Data analysis in 24 patients showed a preoperative BUN level ranging from 9 to 58 mmol (mean value, 21 mmol) and a preoperative creatinine level ranging from 78 to 476 μmol (mean value, 283 μmol). Blood urea nitrogen and creatinine levels increased in the early postoperative period (BUN, mean value of 28.8 mmol, and creatinine, mean value of 330 μmol) in response to the hemodynamic status before implantation, extracorporeal circulation, and surgical stress. Mechanical support seems to improve renal function. In our preliminary data, after seven days of TAH support, the levels of BUN (mean value, 15.1 mmol) and creatinine (mean value, 148 μmol) decreased.

Preoperative pulmonary function was markedly altered in 9 (32.1%) of our patients. Some of them required ventilatory support for several days. Prolonged mechanical ventilation predisposes to infection. In our experience, the lungs were the origin of infection in 35% of the patients who died of sepsis during TAH support.

In addition to preoperative status, the anatomical relation between the TAH and the thorax (left lung compression and atelectasis) could also be responsible for the high rate and severity of the pulmonary infections. Three factors are important in the relation between the TAH and the thorax: thoracic dimension, TAH size, and surgical placement. The anteroposterior diameter measured at the level of the tenth thoracic vertebra, from the anterior surface of the vertebral body to the posterior face of the sternum (DT 10), is the most important anatomical dimension in TAH recipients. In a multiinstitutional study, Jarvik and associates [9] analyzed the relation between

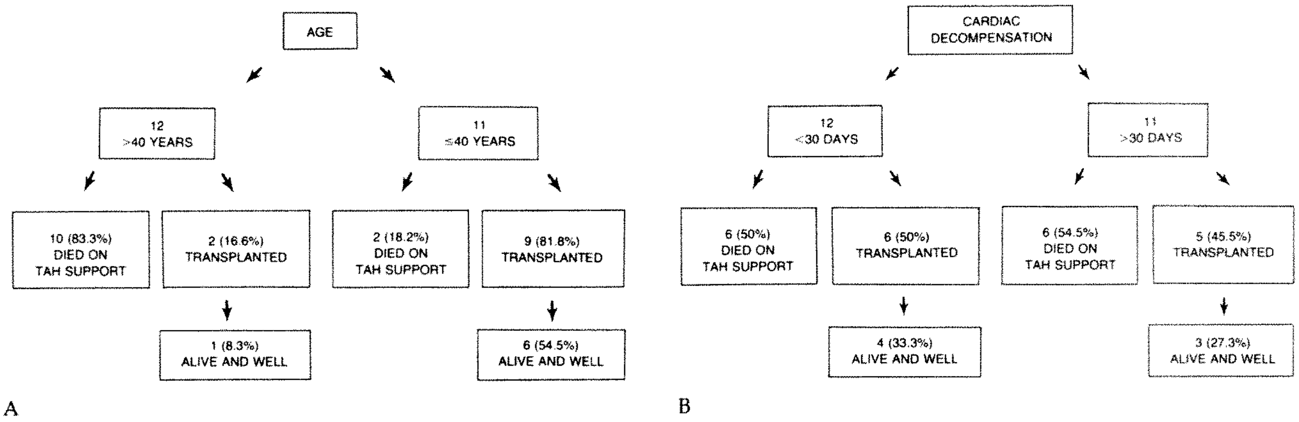


Fig 5. Influence of (A) age on the outcome for patients with total artificial heart (TAH) *support and (B) disease duration on the TAH results.*

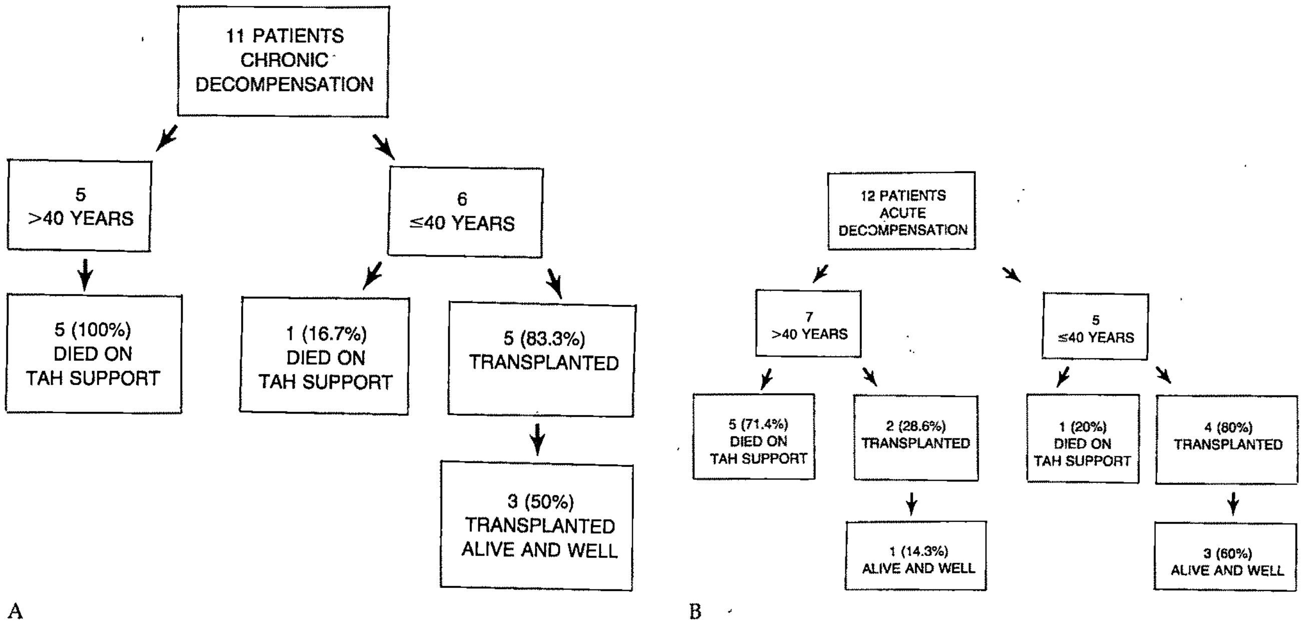


Fig 6. Combined influence of age and evolution of the disease on the short-term and long-term survival: (A) patients with chronic decompensation and (B) patients with acute decompensation.

body surface area and DT 10. They found that a body surface area of 2 m^2 should be used to discriminate between use of the 70-mL Jarvik-7 (body surface area less than 2 m^2) and the 100-mL Jarvik-7 (body surface area greater than 2 m^2). The DT 10 determines the choice between lateral or medial placement of the TAH in the thorax. We believe the lateral position should be avoided, if possible, because it can produce left lung compression and thereby increase the risk of pulmonary infection. All of our implants in patients with a small DT 10 (less than 12 cm) were placed in the medial position without compressing the inferior vena cava and right atrium or causing obstruction of the venous return. In only 1 patient did our evaluation procedure fail, and it was impossible to close the sternum.

Pericardial size may also be important in the fit between the thorax and the TAH. Kolff and Deeb [10] at Temple University studied brain-dead human cadavers and found that in a patient with a normal-sized heart and pericardium, the fit might be too tight for implantation of a 100-mL Jarvik-7. The 70-mL Jarvik-7 might be the device of choice in patients with acute cardiac decompensation and a normal pericardial size.

Our major intraoperative complications were a tear in an atrial cuff and two cases of abnormal function of the diaphragm at the ventricular preimplantation test. In both of the latter instances, the ventricles were replaced. An improper sterilization procedure was found and was suspected of being responsible for the malfunctioning. Both ventricles were sent to the manufacturer for complete evaluation.

There was no postoperative bleeding in our series. A Resorcine Formol Glue used around the sutures in all our implants reduced dramatically the amount of postoperative bleeding.

Coagulation control in TAH recipients was one of the most important problems at the beginning of the clinical experience. At present, many centers are using heparin in association with a platelet inhibitor (aspirin, dipyridamole), and this regimen seems to be more appropriate to control thromboembolism and hemorrhage. Our evaluation of the platelet coagulation and fibrinolytic systems was listed in the Material and Methods section. We used dipyridamole to stabilize platelet activity and aspirin to lower platelet aggregation. When a pathological fibrinolytic state is present, we administer a Kunitz inhibitor (aprotinin) until normalization of the laboratory status and clinical status. There was no clinical evidence of thromboembolic complications during mechanical support in our series, and no clots at the macroscopic level on the explanted devices. Our anticoagulation regimen was also tested in the Material and Methods section.

Analysis of our experience shows that age and acute or chronic terminal heart failure are the most important factors in the survival of TAH recipients. Acute decompensation was defined as rapid deterioration causing terminal heart failure within 30 days before implantation of a TAH. The patients were separated by age into two groups, those older than 40 years old and those younger than 40 years. Data analysis (see Figs 5, 6) revealed that 83% of the patients older than 40 years died under TAH support compared with 18% in the younger group. This difference is also evident when long-term survival is compared; for the older group it was 8.3% and for the younger group, 54.5% (see Fig 5A).

The isolated analysis of acute and chronic decompensation groups failed to demonstrate any difference between these groups. However, when age and evolution of the disease were considered together, their influence on survival became evident. All patients older than 40 years in the chronic disease group died under TAH support, whereas 83% of the younger patients had transplantation and 50% are long-term survivors (see Fig 6A). In the acute decompensation group, there was a difference in survival between the two age groups (see Fig 6B).

One of the most difficult problems in our experience is to identify when a patient has reversible or irreversible organ damage. Renal, hepatic, and pulmonary insufficiency had developed as a result of cardiac failure in most of the candidates for the TAH. Although many of these patients recovered after the implantation of the device, there is a point at which the organ failure becomes irreversible despite correction of the hemodynamic status.

As already described, 11 patients underwent a successful transplant procedure. Five (45.5%) of these patients had an infection in the early posttransplant period, and 2 died of the infection. These data seem to indicate that the infection rate is higher in cardiac transplantation when a mechanical bridging procedure is used. The association between the implantation of the device in a desperately ill patient, a second operation (transplantation) in a short time, and immunosuppression treatment can explain the high early infection rate.

In conclusion, patient selection is the most important factor in TAH results. Early implantation of the device is advised in young patients with acute or chronic cardiac decompensation and in older patients with acute heart failure. Use of the TAH in immunosuppressed patients should be contraindicated because of a high risk of infection. Infection is the most common cause of morbidity and mortality during TAH support. Infection seems to be higher in heart transplantation when a mechanical bridging procedure has been used, but the small number of patients in our series makes any conclusion difficult.

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Interim Use of the Jarvik-7 Artificial Heart: Lessons Learned at Presbyterian-University Hospital of Pittsburgh

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Between October 1985 and March 1988, 16 patients received the Jarvik-7 total artificial heart as an interim device before transplantation. Ten patients were afflicted with cardiomyopathy, and 6 had end-stage ischemic disease. All but 1 were men; the mean age was 47 years (range, 27 to 59 years). Thirteen patients developed cardiogenic shock despite the use of intravenous inotropic agents (mean, 23 days; range, two to 83 days) and the intraaortic balloon pump (mean, 13 days; range, two to 65 days). Three other patients became candidates because of failed transplantation. The 100-mL Jarvik-7 device was used in the first 3 patients; all subsequent recipients were treated with the 70-mL Jarvik-7. Postoperative anticoagulation was designed to keep the partial thromboplastin time between 2 and 2.5 times control. The control values were obtained during administration of heparin and dypyridamole. In all cases the function of the total artificial heart was adequate to support the needs of the recipient, and there were no mechanical difficulties with the device or the drive system. The average time of implantation was 9 days (range, one to 35 days). Two patients died before transplantation, 1 with sepsis from fungus and the other with hemorrhage from a torn pulmonary arterial anastomosis. Fourteen patients received cardiac allografts, and 7 continue to survive without restrictions. Infection within the mediastinum caused the death of 4 patients after transplantation; in 3 of these mediastinitis was not recognized before transplantation but occurred within the first 2 weeks after transplantation. Of the remaining 3 deaths, 1 was due to failure of the donor heart perioperatively, 1 was due to acute rejection in the setting of treated mediastinitis and reduced immunosuppression, and the third occurred during the ninth postoperative month because of medical noncompliance. The Jarvik-7 total artificial heart has been useful in the bridging application and has functioned flawlessly. The current limiting factor of its continued use is the strikingly high incidence of mediastinitis, which does not appear to be related to ascending infection from the drivelines. Our current indications for the use of the device are discussed.

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Between October 1985 and March 1988, 16 patients received the Jarvik-7 artificial heart as an interim device before transplantation. The emergence of total mechanical circulatory support for transplant candidates has occurred because the availability of donor hearts has not kept pace with the increased need for transplantation [1]. Also, it has been demonstrated that the results of transplantation in mortally ill candidates supported by inotropic agents and an intraaortic balloon pump (IABP) have been similar to the greater than 80% 1-year survival possible in recipients having an elective procedure [2, 3]. The key to the good results in the mortally ill has been the selection of candidates for transplantation whose end organs are not irreversibly injured and the exclusion of possible candidates with active infections and marginal hepatic, pulmonary, cerebral, or renal function. We hoped that the Jarvik-7 device could be of benefit to those mortally ill candidates for whom inotropic agents and the balloon pump were insufficient.

The results of the series at Presbyterian-University Hospital of Pittsburgh suggest that although substantial benefit was realized by the 8 survivors of transplantation, many questions have arisen regarding the selection of appropriate candidates and the apparent increased risk of infection in the recipients, especially infection in the mediastinum [4].

Material and Methods

Selection of Patients

The 16 patients who received the artificial heart were candidates for cardiac transplantation. Ten had cardiomyopathy and 6 had end-stage ischemic disease. All but 1 were men with an average age of 47 years (range, 27 to 59 years). Thirteen patients became candidates for the artificial heart when cardiogenic shock developed in spite of the use of intravenous inotropic agents and the IABP (Table 1). The average duration of support with inotropic agents was 23 days (range, two to 83 days); with the IABP it was 13 days (range, two to 65 days). These patients were judged not likely to survive a few hours, and once the decision to implant the device was made, the procedure was conducted emergently (Table 2).

The cardiac index in these 13 recipients ranged from less than 1.0 to 1.4 L/min/m^2. All had some degree of

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Table 1. Indications for Use of the Artificial Heart in 16 Patients

Indication	No. of Patients	Transplanted	Alive
Cardiogenic shock while waiting for donor heart	13	11	7
Acute rejection of donor organ (within 24 h of transplantation)	1	1	1
Primary failure of donor heart	2	2	0

mental obtundation, which was severe in 3. Before selection, high doses of diuretics were required to maintain hourly urinary outputs of 10 to 50 mL/h; 1 patient was anuric. The serum creatinine concentration averaged 2.0 mg/dL (180 μmol/L) and ranged from 1.1 to 4.1 mg/dL (97 to 360 μmol/L). Acute pulmonary edema was noted radiographically in these 13 candidates awaiting their first cardiac transplant, and 4 of them required urgent preoperative tracheal intubation and mechanical ventilation.

When it appeared that medical treatment and intraaortic counterpulsation were failing, an attempt was made to discuss the possible need for the artificial heart before the clinical condition deteriorated. Informed consent for the use of the artificial heart was obtained in advance or at the time of implantation from 4 recipients and from all of the families.

The decision to implant the total artificial heart (TAH) was prompted by a progressive decline in cardiac function, which was associated with cardiopulmonary resuscitation in 12 patients. One patient had cardiac arrest in another hospital, where a biventricular support system (Bio-Medicus) was implanted to maintain the patient's life. Later the patient was transferred to Presbyterian-University Hospital for substitution of the Jarvik-7 and subsequent transplantation.

Three patients became candidates as a consequence of failed transplantation (see Table 1). In 1 recipient, the need to bridge occurred because of the inexplicable failure of a donor heart to function 12 hours after transplantation. In another patient, a donor heart was belatedly found at the time of its planned implantation to have extensive myocardial contusion with atrial septal rupture not diagnosed because of inadequate echocardiographic and physical examinations at the referred hospital. In 1 patient, hyperacute rejection of the heart developed within an hour of transplantation, presumably because of rare preformed antiendothelial antibodies to the donor, which were found to be present retrospectively (Fig 1) [5].

Our current contraindications to implantation have evolved from experience gained throughout the bridging trial (Table 3). In general, the device should not be used to resurrect patients from death but should be applied when there exists a reasonable chance for survival, not only early after implantation but through transplantation. Patients are not selected unless at the moment of implantation they are considered candidates for cardiac transplantation were a donor heart available. Every attempt is made to exclude candidates with active infection. We have found that hypotension associated with sepsis can be difficult to distinguish from progressive cardiogenic shock in the mortally ill candidate. The infectious origin of shock that occurred in 2 candidates on the IABP was misdiagnosed, and sepsis continued after implantation of the TAH. Although anuria was present in 2 recipients, it was of short duration (less than two hours), and patients with established acute tubular necrosis were not chosen.

Because a third of our recipients required reoperation for hemorrhage, those with previous sternotomies are not considered because of the additional risk of bleeding from lysed adhesions in the anticoagulated recipient. Patients weighing less than 51.75 kg with an anterior vertebral (T-10) to sternal distance of less than 8 cm are likely to pose "fit" problems, even if the 70-mL Jarvik-7 is used and the right ventricle is positioned to the left of the midline (Fig 2). The presence of preformed antibodies to human lymphocyte antigens (percent reactive antibody greater than 20%) increases the likelihood of extending the bridge experiment to a chronic one because of an inability to find a compatible donor heart. Finally, we have learned in two instances that unresponsive or coma-

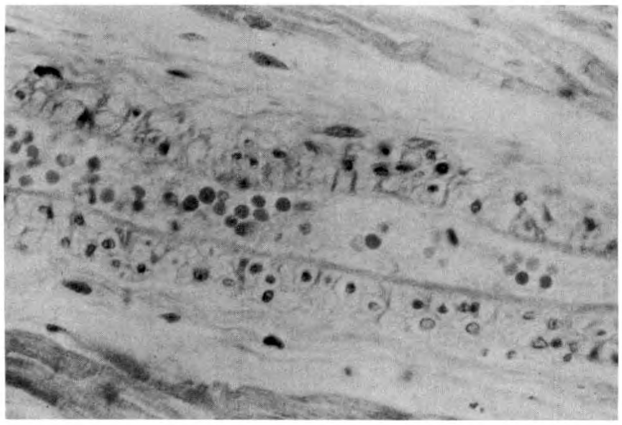

Fig 1. Photomicrograph of hyperacute rejection showing capillary occlusion with platelet thrombi.

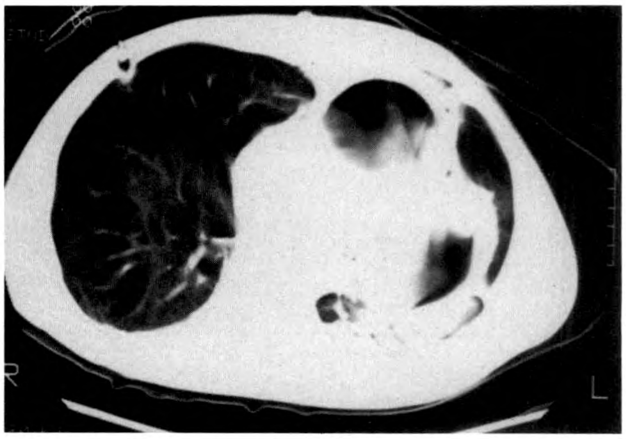

Fig 2. Surgical positioning of the total artificial heart entirely to the left of midline, which effectively avoids systemic and pulmonary venous obstruction.

Table 2. Summary of Data on 16 Patients Given the Total Artificial Heart

Variable	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Indication	Cardiomyopathy	Acute infarction	Cardiomyopathy	Cardiomyopathy	Ischemic heart disease	Acute intraoperative rejection	Unexpectedly injured donor heart
Intravenous inotropic drugs (days)	33	7	10	54	11	. . .	12
Intraaortic balloon pump (days)	22	3/2[a]	5	15	1	. . .	1
Preimplantation cardiac index (L/min/m^2)	1.1	<1.0	1.3	1.4	. . .	1.1	. . .
Serum creatinine (mg/dL)[b]	1.6	1.1	4.1	1.3	1.8	2.0	0.7
Eight-hour urine output (mL)	275	300	100	250	0	. . .	700
Bilirubin (mg/dL)[b]	1.1	1.3	8.0	2.1	6.4	1.5	1.0
Radiographic pulmonary edema	Yes	Yes	Yes	Yes	Yes	. . .	No
Mental obtundation	Mild	Moderate	Severe	Mild	Moderate	. . .	None
Days with implant	4	13	18	2	6	9	2
Outcome	Home for 10 mo	Home for 6 mo	Died[c]	Died[d]	Home for 3 mo	Home for 3 mo	Died, cause unknown

[a] A biventricular assistance device was used for two days. [b] To convert values for creatinine and bilirubin to micromoles per liter, multiply by 88.4 and 17.1, respectively. [c] Patient died of candidal sepsis and multiorgan failure. [d] Patient died of rejection 60 days after transplantation.

tose patients are poor candidates because of an uncertain prospect for neurological recovery. Such recovery is especially important to assess after cardiopulmonary resuscitation.

Operative Procedure and Postimplantation Care

The operation is performed through a median sternotomy. The pericardium is not removed. The pneumatic drivelines exit through skin incisions below the left lateral costal arch at the anterior axillary line. The aim is to position the artificial heart so that the left ventricle is drawn inferiorly and laterally and the right ventricle is pulled to the left of the sternum anteriorly. In smaller recipients, this prevented obstruction of pulmonary and systemic venous return and permitted closure of the sternum, but necessitated placement of the left ventricle in the left pleural space (see Fig 2). The 100-mL Jarvik-7 device was used in the first 3 patients, and the 70-mL or "mini" Jarvik-7 was used in the last 13 because we found that it was easier to implant and could be used in large and small recipients.

All patients remained in the surgical intensive care unit, and the function of the artificial ventricles was monitored by the cardiac diagnostic unit that is integral to the Utah heart drive console. For the first 12 to 24 hours, a physician, usually a surgical resident from the surgical research laboratory, remained at the bedside; thereafter, the physician was immediately available by page from within the hospital. Information from the cardiac monitor was monitored by a technician, and concerns were communicated to the investigators. Direct connection to the cardiac output monitor diagnostic unit was made possible

Table 3. Contraindications to Bridging to Transplantation With the Jarvik-7 Artificial Heart

Contraindication	Explanation
Presence of active infection	Infection after implantation
Previous sternotomy	Hemorrhage from lysed adhesions in anticoagulated recipient
Age > 60 years	Reasonable expectation of survival and limited other secernent systemic illnesses
Evidence of preformed antibodies to human lymphocyte antigens (percent reactive antibody > 20)	Increased likelihood of not finding compatible donor after implantation
Established acute tubular necrosis	High risk of postimplantation and transplantation difficulties
Unresponsiveness or coma	Risk of implanting device in patient with poor prospect of neurological recovery
Small size, weight < 51.75 kg, vertebral-sternal dimension < 8 cm	Poor fit of device with high likelihood of pulmonary and/or systemic venous obstruction

Table 2. Continued

Patient 8	Patient 9	Patient 10	Patient 11	Patient 12	Patient 13	Patient 14	Patient 15	Patient 16
Cardiomyopathy	Cardiomyopathy	Cardiomyopathy	Ischemic heart disease	Cardiomyopathy	Ischemic heart disease	Cardiomyopathy	Failure of donor heart	Ischemic heart disease
11	2	3	18	28	41	13	13	83
2	1	2	8	16	41	1	. . .	65
1.6	1.7	1.2	1.2	1.5	1.7	1.76	3.6	1.8
1.6	2.6	2.2	1.3	2.5	2.5	1.5	1.2	2.5
180	0	300	620	300	500	30	450	500
7.3	4.3	1.3	5.4	4.1	0.6	1.1	1.0	1.9
Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Mild	Mild	Severe	Moderate	Moderate	Mild	None	Severe	Mild
8	4	4	5	35	13	6	7	1
Home for 16 mo	Home for 16 mo	Died, cause unknown	Died, infection	Died, infection	Died, infection	Home for 10 mo	Died, infection	Died, hemorrhage

by telephone modem. Anticoagulation with heparin sodium and dipyridamole was started as soon as the mediastinal drainage slowed, usually within eight hours of the operative procedure. Intravenous administration of heparin was initially begun at a dose of 500 units per hour, and the dose was increased hourly until a partial thromboplastin time between two and two and a half times the control value was reached. Dipyridamole, 75 mg, was given by nasogastric tube or by mouth every eight hours.

Our inclination was to substitute a donor heart for the TAH as soon as circumstances became reasonable. On occasion, patients were not listed as priority candidates for cardiac transplantation for a few days so that pulmonary edema, renal insufficiency, mental obtundation, or any combination of these could resolve or stabilize. Although we considered renal insufficiency and failure undesirable before transplantation, we believed that relative to other problems previously shown to be associated with long-term use of the TAH, they would not be a contraindication. The only absolute contraindication to transplantation was uncontrolled infection.

The immunosuppressive regimen followed after transplantation was similar to that used in routine cases except that azathioprine was avoided. All patients received 500 mg of methylprednisolone when the transplanted organ was reperfused and 125 mg every eight hours for three doses. Thereafter, except for treatment of acute rejection, steroids were limited to 20 mg of prednisone daily. Cyclosporine was withheld preoperatively and begun at a dose of 2.5 mg/kg every 12 hours in the first few postoperative hours when the patient was in stable condition and exhibited adequate cardiac and renal functions. The dose was usually adjusted upward to a targeted whole blood level (radioimmunoassay, Sandoz, Ratan, NJ) of 700 ng/mL. Some consideration of a lowered dose was made for those individuals with abnormal renal function. Polyvalent antithymocyte globulin made from rabbits in the surgical laboratory was given intramuscularly for five days.

Results

Function of the Jarvik-7 Device

The drive pressure, heart rate, and percentage of systole were adjusted to ensure complete ejection of blood from the ventricles (Table 4) [5]. Most of our experience has been with the 70-mL device, and we previously compared its function with the larger 100-mL heart [6]. The 70-mL Jarvik-7 produced physiological cardiac outputs that

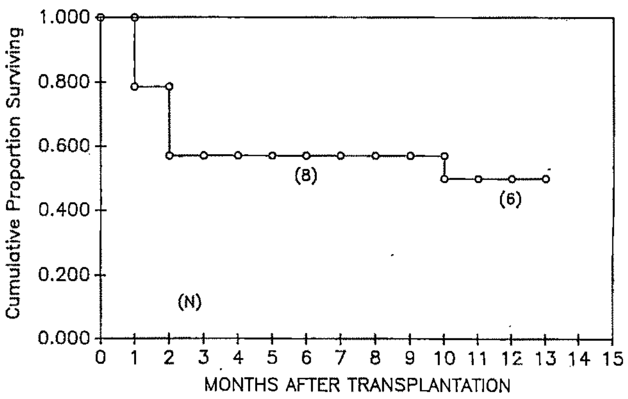

Fig 3. Total artificial heart bridge-to-transplantation survival at the University of Pittsburgh.

Table 4. Functioning and Effects of the Total Artificial Heart in 16 Patients

Variable	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Jarvik-7 used	100 mL	100 mL	100 mL	70 mL	70 mL	70 mL	70 mL
Cardiac output (L/min)	6–7	5–6.5	5–7.5	5.5–7	5–6	5–6	3.0–6.6
Left driveline pressure (mm Hg)	150–160	160–175	180–195	155	180	175–180	165–185
Right driveline pressure (mm Hg)	60	50	55	60–77	50	50–60	55–80
Heart rate (beats/min)	84	85	120	90	115	110	110–115
Central venous pressure (mm Hg)	10–15	10–15	10–20	10–12	7–12	8–12	8–16
Left atrial pressure (mm Hg)	7–10	12–14	8–16	6–10	5–10	7–10	5–10
Plasma-free hemoglobin (mg/dL)	. . .	14	1–14	. . .	2.5	1.8–20	37.5
Lactate dehydrogenase (IU)	481	691	671	450	453	529	. . .

ranged between 2.7 and 8.8 L/min at heart rates between 84 and 125 beats per minute. Left-sided and right-sided filling pressures corresponded to left atrial pressures of 7 to 16 mm Hg and central venous recordings of 5 to 25 mm Hg. The use of vacuum during diastole, especially at heart rates higher than 110 beats per minute, improved cardiac output by at least 15% to 20% and resulted in a corresponding decrease in venous pressures. Most recipients were managed with cardiac outputs of 4 L/min at heart rates of 115 beats per minute and venous pressures of 10 mm Hg. Transient rises in central venous pressure and left atrial pressure occurred during coughing, during endotracheal suctioning, and when patients became animated with visitors. None of these episodes required a change of the drive functions. After the first 24 hours of support, heart rate and left and right drive-pressure settings required little or no adjustment, even when the patient changed from a supine to an erect position. The rate of rise of left ventricular pressure of our drive console was maintained at 2,500 mm Hg/s, serious hemolysis did not occur, and plasma hemoglobin concentrations never rose above 20 mg/dL. Thrombocytopenia occurred in 2 patients. One had candidal sepsis, and in the other, thrombocytopenia developed after 24-hour biventricular support with Bio-Medicus pumps.

Survival

The average length of time of implantation was 8.71 days (range, 1 to 35 days). The actuarial survival of our patients who received the TAH was 50% (Fig 3). Two of the 16 patients died before transplantation, 1 of sepsis from fungus and the other of hemorrhage from a torn pulmonary arterial anastomosis (Table 5). Fourteen patients received cardiac allografts, and 7 are alive without restrictions. Infection within the mediastinum caused the death of 4 patients after transplantation. In 3 of these patients, mediastinitis was not recognized before transplantation but occurred within the first 2 weeks after operation. Of the remaining 3 deaths, 1 was due to sudden and still unexplained failure of the donor heart on the first postoperative day and another on the 60th postoperative day in the setting of reduced immunosuppression and treated mediastinitis. Another occurred late during the ninth postoperative month and was due to medical noncompliance.

Infection

Six of the 9 deaths were related to infection [4]. One patient died of bacterial and fungous sepsis before transplantation, and 5 died of mediastinitis. In only 1 of these patients was mediastinitis diagnosed before transplantation. This patient had transplantation on the 36th day after implantation with evidence of persisting localized mediastinitis, and died promptly of sepsis. The diagnosis was made early after transplantation by culture of pericardial and pleural fluid, except in the only successfully treated patient, in whom a localized infection was detected 3 weeks after transplantation.

Infected sputum or frank pneumonia occurred in all 6 patients who died of infection. In 3 of these patients, the same organism appeared to be related to the subsequent mediastinitis (*Serratia marcescens*, 2; *Pseudomonas*, 1), and in 1 patient it caused sepsis (*Enterobacter aerogenes* and *Candida albicans*) that resulted in death before transplan-

Table 5. Deaths With Temporary Artificial Heart

Cause	During Implantation	After Transplantation
Infection	1	4
Bleeding	1	0
Medical noncompliance	0	1
Failure of donor heart	0	1
Rejection of donor heart	0	1[a]
Total	2/16	7/14

[a] This occurred in the setting of reduced immunosuppression with mediastinitis.

Table 4. Continued

Patient 8	Patient 9	Patient 10	Patient 11	Patient 12	Patient 13	Patient 14	Patient 15	Patient 16
70 mL	70 mL	70 mL	70 mL	70 mL	70 mL	70 mL	70 mL	70 mL
4.7–8.8	3.6–8.6	4.4–6.9	4.3–8.0	4.1–8.7	3.3–7.7	3.7–7.9	2.7–7.2	2.7–7.0
175–195	160–210	150–165	150–180	150–185	160–190	165–190	175–210	180
40–60	60–80	50–60	45–70	50–80	50–80	60–70	60–85	75–100
102–120	115–125	110–115	115–125	115–120	105–115	88–125	110–120	110–125
5–16	5–22	4–14	4–18	5–25	6–17	6–15	9–18	11–18
8–16	5–20	5–15	3–14	5–16	3–10	. . .	3–18	. . .
1–14	0–15	3–53	2–24	1.8–10.3	0.8–6.0	4–7	1–20.3	57
227–285 (264)	424–502	352–1,038	349–430	266–446	283–449	275–449	397–746	. . .

tation. The 2 additional cases of infection were due to *Mycoplasma hominis*, a bacteria difficult to isolate from the sputum but known to reside within the respiratory system. For all 6 patients, the cultures of the mediastinum obtained during the transplant procedure were sterile except for the 1 with mediastinitis and pneumonia from *Pseudomonas*. Within the second to 22nd posttransplant day, intrathoracic cultures became positive. An ascending infection from the pneumatic drivelines was not detected in any of the patients. The inside of the TAH was infected by *Candida albicans* in the patient who died of bacterial and fungous sepsis before transplantation. In this case, endocarditis-like lesions were found adjacent to the outflow valves and within the aortic and pulmonary conduits.

Factors including age, number of sternotomies, duration of implantation of the TAH, days of support on the mechanical ventilator before infection, and duration of preoperative use of inotropic agents and the IABP were assessed to determine their possible influence on subsequent lethal infections [4]. Although patients with infection were older and required longer preoperative periods of support, the differences did not reach significance. The number of days on mechanical ventilation and the requirement for a repeat sternotomy because of bleeding were essentially the same in both groups. Acute renal failure frequently accompanied septic complications and was believed to be a result of the infection, not the cause.

We have found that the noninfected surviving patients have been able to mount a response against the donor heart. The actuarial freedom from rejection was 46% at 3 months, and did not differ from a group of routine transplant recipients treated with similar immunosuppression. In 1 of our bridged patients, moderate rejection of the allograft developed in the setting of reduced immunosuppression for treatment of healing mediastinitis. The rejection process worsened and caused death on the 60th posttransplant day. The interrelationship between protection from infection and rejection remains obscure, but clearly an overall reduction of immunosuppression is not likely to be possible.

Thrombosis and Thromboembolism

Cerebral embolism occurred in 1 patient who was receiving a large dose of heparin (1,200 U/h) but whose partial thromboplastin time was only 37 seconds (control, 30 seconds). Most explanted devices showed some deposition of small thrombi (1 to 3 μm in diameter) in the inner and outer crevices formed between the polished valve rings and their isoplastic housings (Fig 4A) and occasionally in the groove formed by the graft valve housings (Fig 4B). These findings occurred variably in the major and minor orifices of the atrioventricular, aortic, and pulmonary valves. In two 100-mL Jarvik-7 hearts, large red thrombi were found; one was loosely adherent to the suture line connecting the left atrium to the polyurethane-covered inlet cuff (Fig 4C), and the other adhered to the polyurethane diaphragm at its point of connection to the rigid left ventricular housing (Fig 4D). There was no evidence of wear to the valves, housings, or blood and air diaphragms.

Although thromboembolism has been a major potential problem, we have studied the rheology of the blood in our recipients to determine whether there are abnormalities of the red blood cells caused by exposure to the device that result in abnormally stiff or poorly deformable cells. Altered blood rheology characterized by elevated blood viscosity, fibrinogen, and red cell rigidity has been found in all patients [7]. The measured increase in red blood cell rigidity suggests that the TAH alters the overall biomechanical properties of these cells, in particular the cellular membranes. We have shown by analysis of regional xenon blood flow that our TAH-supported patients have a significant reduction in cerebral perfusion relative to that measured after transplantation in spite of higher cardiac outputs during the period of mechanical support [8]. When coupled with elevated viscosity and fibrinogen concentrations, it is possible that the measured rheological abnormalities cause an increase in resistance to flow in the microcirculation, resulting in impaired organ perfusion.

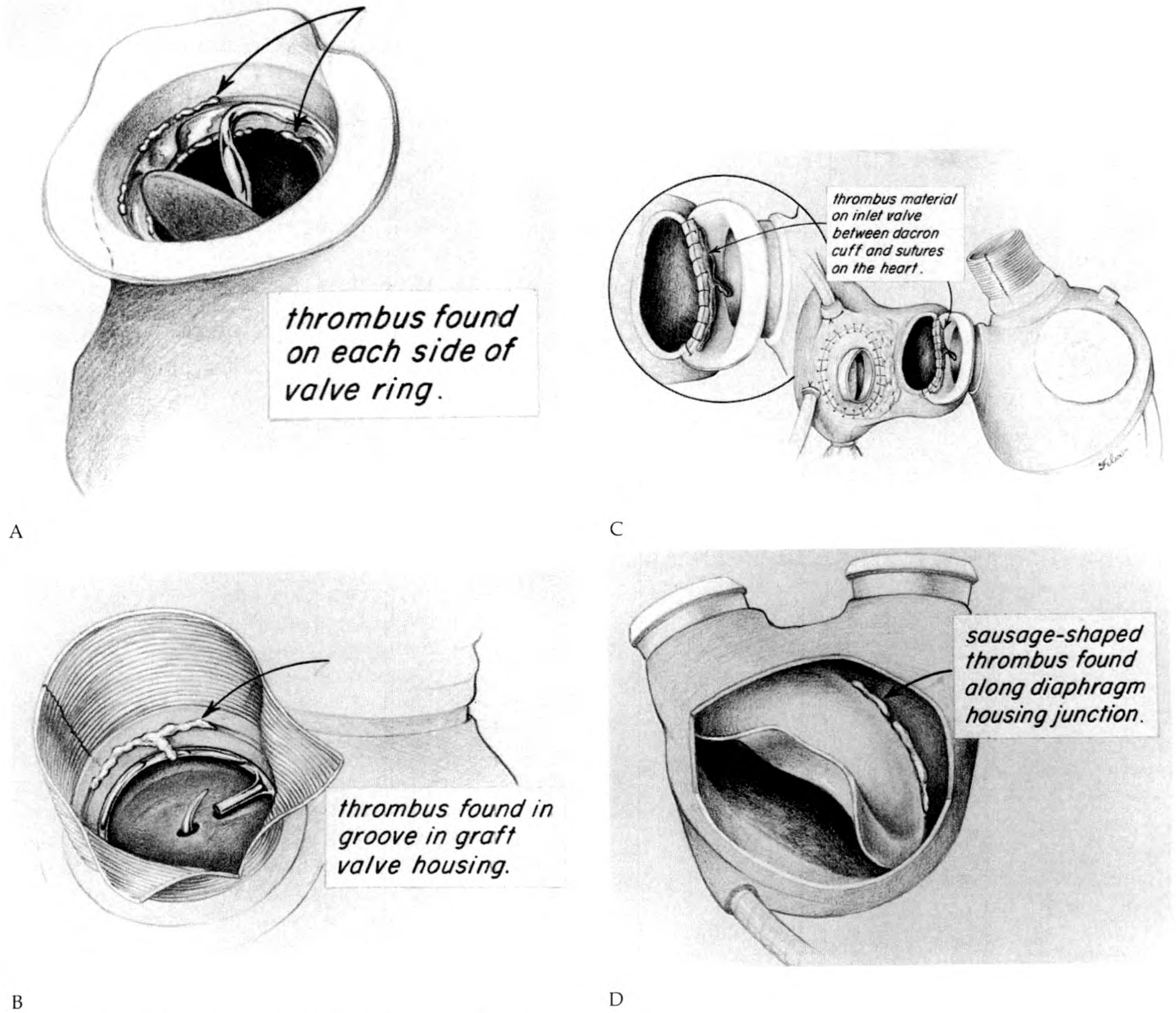
thrombus found on each side of valve ring.
A
thrombus material on inlet valve between dacron cuff and sutures on the heart.
C
thrombus found in groove in graft valve housing.
B
sausage-shaped thrombus found along diaphragm housing junction.
D

Fig 4. Examples of thrombi found in the explanted artificial hearts.

Comment

The use of the TAH as a bridging device has caused criticism because this application increases the number of mortally ill candidates waiting for donor hearts and leads to poorer results after transplantation relative to those possible in nonroutine recipients [9]. The actuarial survival of all recipients of the TAH (Unger heart) in Pittsburgh has been 50% (see Fig 3), a result significantly lower than the 85% national average first-year survival after heart transplantation alone. Advocates of the experiment counter that temporary use of the devices is ideal, as valuable information can be learned that ultimately might benefit a large number of patients when clinical strategies and technology progress to produce a more therapeutic permanent device [10, 11].

We have chosen to be conservative in selection and currently include candidates with reasonably recoverable situations; we prefer not to use the heart as a triage for large numbers of patients who may or may not recover enough to become transplant candidates. Experts agree that the key to the selection of candidates likely to ultimately benefit from the bridge is an understanding that the TAH should not be used to resurrect dying patients from prolonged cardiopulmonary arrest or advanced degrees of renal and hepatic failure, and should not be used in those with any evidence of coexisting sepsis or pneumonia [11]. The rates of survival after transplantation indicate our perhaps ill-advised preference to be more aggressive with transplantation in those with implantation-related complications, including pneumonia, mediastinitis, and renal failure. This preference suggests our unwillingness to date to become involved in a complicated, chronic implant situation with minimal hope for therapeutic results.

There have been four major complications subsequent to implantation of the TAH as a bridge: perioperative hemorrhage, thromboembolism, infection, and multiorgan failure [4, 12, 13]. Up to a third of these patients have required a return to the operating room to address excessive perioperative bleeding. The problem is due to multiple suture lines and the requirement for aggressive use of early therapeutic anticoagulation out of fear of thromboemboli from the Jarvik-7 device. The relatively low (1 of 16) but still unacceptable rate of thromboembolic phenomena in this application of the device compared with that occurring with its permanent use is due to good fortune, its short-term application (mean, 13 days), and an aggressive protocol of anticoagulation based on the lessons learned from DeVries [14]. It is likely that pumps of better design will lessen the risk of stroke, but based on the experience of DeVries, the threat of embolism from pseudoendocarditis will continue [15, 16].

Most investigators were aware of a substantial risk of infection with the interim use of the TAH, as lethal infection had been the cause of death in every long-term survivor of the permanently implanted TAH. Because clinical and animal infections generally were diagnosed after 4 weeks, it was hoped they could be minimized by restricting the time of implantation to 14 to 21 days. Although all investigators have noted significant mortality due to infection, the Pittsburgh series is most remarkable for a staggering 31% incidence (5/16) of mediastinitis, which was diagnosed in all but 1 patient early after transplantation [6]. Deep infection of the skin buttons with spread to the periprosthetic space has not been noted in the bridged patients who have received donor hearts within 2 to 4 weeks of implantation, probably because of the relatively short duration of implantation.

Our series suggests no difference in rates of survival between the routine transplant population who were admitted for an operative procedure and those with prolonged hospitalization who were supported on inotropic agents and the IABP. Our balloon-supported patients, however, have had an increase in nonlethal infections after transplantation (Table 6). It was noted that recipients of the TAH in whom lethal infections developed tended toward longer periods of preoperative support with inotropic agents (12 versus 30 days) and the IABP (3.4 versus 17 days), but like age (45 versus 47.5 years), these differences were found to be not significant [6]. We have noted that patients have been able to mount an immune response against the transplanted organ, but we believe that this response is not directly related to similar inclinations against infection.

It is most likely that the pericardial space, which contains clotted blood and serum plus the prosthetic ventricle and vascular conduits, represents a major problem for local host defense against infection [4]. Realistically, in the bridged patient almost every potential factor known to contribute to surgical infection is present, and perhaps one might question why the incidence of lethal infection is not higher. Based on the successful use of paracorporeal ventricular assist devices, it would seem that maintenance of a beating heart and epicardial-to-pericardial apposition is a major benefit [17].

Continued work with the temporary orthotopic replacement of the native heart with a mechanical heart is necessary to provide insight into problems and solutions critical to expansion of this important technology. In the future, we plan to exclude all candidates for the TAH who are being treated for infection; to move more quickly so as to avoid the hopelessly ill candidate; to reduce the level of anticoagulation early postoperatively to lessen the risk of bleeding and repeat sternotomy; to experiment with the use of antibiotics to selectively decontaminate the gastrointestinal tract of aerobes and fungi in an effort to reduce bacterial translocation and enteric pneumonias; to eliminate the pericardial space as much as possible; and to consider the use of omental wraps and perhaps sustained-release antibiotics around the TAH. Although an overall reduction in immunosuppression is not likely to lead to benefits because the risk of rejection appears similar to that in routine transplant recipients, we are pursuing a strategy of less immunosuppression early on, with augmentation at 2 to 3 weeks after transplantation when the risk of infection in the wound is lower. The initial experience with the temporary use of the TAH has benefited many recipients and has prompted us to continue its selective application.

Table 6. Role of Infection in Heart Transplant Recipients

Recipient Population	No. of Patients	Nonviral Infection	Death Due to Nonviral Infection
Elective	183	53 (29%)	8 (4%)
Mortally ill			
Intravenous inotropic agents	78	24 (31%)	2 (3%)
Intraaortic balloon pump	57	26 (46%)	3 (5%)
Artificial heart	16	14 (88%)	6 (38%)

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Bridging to Cardiac Transplantation

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Unilateral or bilateral prosthetic ventricles and artificial hearts have been used in bridging to transplantation for 4 years. Candidates for bridging to transplantation comprise patients who otherwise would be elective cardiac transplantation candidates who deteriorate rapidly before a donor heart can be found, or persons with sudden cardiac decompensation (eg, massive myocardial infarction with cardiogenic shock). In selecting patients for bridging to cardiac transplantation it is crucial that people are chosen who are good candidates for heart transplantation despite their rapidly deteriorating condition. This article compares the results of the devices available for use in this application, which include: the centrifugal pump; the Jarvik-7 orthotopic prosthetic ventricle; and the Thoratec, Novacor, and Thermedics heterotopic prosthetic ventricles.

(Ann Thorac Surg 1989;47:167–71)

The modern era of bridging to cardiac transplantation using prosthetic ventricles began in 1984 [1–3]. Bridging to transplantation is a two-step procedure: implantation of the device and then orthotopic cardiac transplantation. Success in device implantation is dependent on three elements: patient selection, surgical skill in performing a new, nonstandardized operation, and a risk-free prosthetic blood pump. The success of step two, orthotopic cardiac transplantation, in a bridge situation depends on the same three elements: patient selection, skillful surgical technique, and a posttransplantation period free from latent device-related complications. There continues to be a substantial learning curve associated with this procedure, the most important part of which relates to patient selection. This is discussed extensively in other papers presented at this symposium.

A number of devices originally designed for permanent cardiac support are being used in bridging to cardiac transplantation. Here I present the cumulative early results with this procedure and the experience with a variety of devices.

Material

Cardiac Support Devices

Three categories of devices are reported: centrifugal pumps, orthotopic prosthetic ventricles (total artificial heart), and heterotopic prosthetic ventricles (ventricular assist devices). Roller pumps have also been used successfully; however, the reports are isolated and no cumulative record of the number of attempts and their outcome exists. Examples of the various pumps in each category are as follows:

- Category 1: Centrifugal Pumps
  - Bio-Medicus
  - Centrimed
  - Medtronic
- Category 2: Orthotopic Prosthetic Ventricles
  - Jarvik heart
  - Penn State heart
  - Utah heart
  - Unger heart
  - Berlin heart
- Category 3: Heterotopic Prosthetic Ventricles
  - Abiomed
  - Novacor
  - Symbion
  - Thermedics
  - Thoratec

Table 1 lists their status with the US Food and Drug Administration (FDA) at the time of this report (February 1988). This status is subject to change with additions and deletions, and should not be interpreted as currently applicable.

The purpose of this report is to review data on five devices being investigated for use in bridging to transplantation. Not included are devices that have been used only once or twice. Detailed descriptions of the various pumps and techniques of implantation can be found in other symposium papers.

Patients

There were no standardized entry criteria for the different groups of patients constituting the data base for this analysis. The generally accepted indication for bridging to transplantation is a patient who is within minutes or hours of death, who has none of the standard contraindications to cardiac transplantation, and for whom the probability of locating an acceptable donor organ is good. The end points in this analysis are reaching step two, transplantation, and discharge from the hospital. There

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Table 1. Status of Pumps Under the FDA Investigational Device Exemption Regulations

Pump	Bridge	Recovery
Abiomed	. . .	OK
Berlin heart	. . .	. . .
Centrifugal	. . .	. . .
Bio-Medicus		
Centrimed		
Jarvik (total)	OK	. . .
Novacor	OK	OK
Penn State heart	OK	. . .
Symbion (LVAD)	. . .	OK
Thermedics	OK	OK
Thoratec	OK	OK
Unger heart	. . .	. . .
Utah heart	. . .	. . .

LVAD = left ventricular assist device.

were no standardized protocols for patient management among the various clinical centers that did the investigations. When available, I have included both the medical reasons for failure to reach the two goals and the device-related complications.

The centrifugal pumps are reported together. The data source is the Clinical Registry of Mechanical Ventricular Assist Pumps and Artificial Hearts of the International Society of Heart Transplantation and the American Society of Artificial Internal Organs. This registry has a voluntary reporting system and therefore does not include all procedures done. The remaining data were obtained directly from the device manufacturers. This information is inclusive and originates from the data base reported to the FDA. With the exception of centrifugal pumps, these devices are all controlled by the FDA in clinical trials under the investigational device exemption (IDE) regulations.

Results

Centrifugal Pumps

The results of using centrifugal pumps as a bridge to transplantation are shown in Table 2. Sixteen (64%) of the 25 patients placed on a centrifugal pump underwent transplantation, and 10 (62.5%) of the 16 were discharged from the hospital. The overall survival was 40%. Of the 25 patients treated, 11 (44%) had biventricular and 14 (56%) had univentricular support (1 patient had right ventricular support and the remaining 13 had left ventricular support).

Table 2. Bridging to Transplantation Results With Centrifugal Pumps[a]

Device	Implanted	Transplanted	Transplant Survival	Overall Survival
LVAD	13	9	7	7
RVAD	1	1	1	1
BIVAD	11	6	2	2
Total	25	16 (64%)	10 (62.5%)	10 (40%)

[a] These are the Bio-Medicus, Centrimed, and Medtronic pumps.

BIVAD = biventricular assist device; LVAD = left ventricular assist device; RVAD = right ventricular assist device.

Table 3. Complications Seen With Centrifugal Heart Pumps

Complication	Transplanted (n = 16)	Not Transplanted (n = 9)	Total (n = 25)
Bleeding	8	8	16 (64%)
Renal failure	5	7	12 (48%)
Infection	4	5	9 (36%)
Hemolysis	4	3	7 (28%)
Respiratory failure	2	4	6 (24%)
Thrombosis (device)	2	3	5 (20%)
Biventricular failure	2	3	5 (20%)
Inadequate cardiac output	2	2	4 (16%)
Perioperative infarct	2	2	4 (16%)
Neurological	1	3	4 (16%)
Emboli	1	1	2 (8%)
Cyanosis	1	1	2 (8%)
Disseminated intravascular coagulation	0	1	1 (4%)
Mechanical failure: cannula obstruction	0	0	0
Intraaortic balloon	0	0	0
Other	4	1	5 (20%)

The incidence of serious complications was high (Table 3). Bleeding, renal failure, infection, hemolysis, respiratory failure, and thrombosis were the most common and contributed substantially to mortality.

Orthotopic Prosthetic Ventricles (Total Artificial Heart)

Jarvik orthotopic prosthetic ventricles were implanted in 81 patients. Fifty-eight patients (72%) went on to cardiac transplantation, and of those, 31 (53%) were discharged from the hospital. Overall survival was 31 of 81 patients or 38% (Table 4). Twenty-three patients died or had contraindications to transplantation during the device-support period. The predominant causes of death were multiorgan failure and infection. Infection was also a leading cause of death among the 27 patients who did not survive cardiac transplantation. There are no specific data on device-related complications.

Heterotopic Prosthetic Ventricles, Univentricular and Biventricular

NOVACOR HETEROTOPIC UNIVENTRICULAR LEFT PROSTHETIC VENTRICLE. The Novacor prosthetic ventricle was implanted in 17 patients. Seven patients (41%) underwent transplantation, and 5 (71%) survived. The overall survival was 29% (see Table 4).

At the time of writing, 1 of the 10 patients not having

Table 4. Overall Survival With Various Pumps

Pump	No. of Patients	Transplanted	Discharged	Overall Survival
Centrifugal	25	16 (64%)	10 (62.5%)	10 (40%)
Jarvik (total)	81	58 (72%)	31 (53%)	31 (38%)
Novacor	17	7 (41%)	5 (71%)	5 (29%)
Thermedics	4	3 (75%)	1 (33%)	1 (25%)
Thoratec	57	46 (81%)	38 (83%)	38 (67%)

transplantation was awaiting a donor. The medical reasons for disqualifying the remaining 9 patients are listed in Table 5. Once again, multiorgan failure was the principal cause. The cause of death in the 2 patients who did not survive transplantation was sepsis in 1 and right ventricular graft failure in the other. The device-related complications are listed in Table 6. There were three infections that were managed successfully and two strokes that were related to device implantation.

THERMEDICS HETEROTOPIC UNIVENTRICULAR LEFT PROSTHETIC VENTRICLE. Four patients were treated using the Thermedics prosthetic ventricle. Three (75%) underwent transplantation and 1 (33%) survived. The overall survival was 25% (see Table 4). Multiorgan failure developed in the 1 patient who did not undergo transplantation. The 2 deaths after transplantation were due to multiorgan failure and graft failure. There were no device-related complications (Table 7).

THORATEC HETEROTOPIC UNIVENTRICULAR AND BIVENTRICULAR PROSTHETIC VENTRICLES. Fifty-seven patients with terminal cardiac failure were treated with Thoratec prosthetic ventricles. The mean age was 41 years (range, 13 to 58 years). Forty-seven (82%) were male, and 10 (18%) were female. Heart failure attributable to coronary artery disease was the cause in 29 (51%), and cardiomyopathy accounted for the remaining 28 (49%). A left prosthetic ventricle was used in 12 patients (21%) and biventricular devices in 45 (79%) (Table 8). The site of left ventricular cannulation was fairly evenly divided between the left atrial appendage (35%), the left atrial roof adjacent to the right superior pulmonary vein (37%), and the left ventricular apex (28%). The mean duration of support was 8.5 days, with a maximum of 74 days. Twenty-nine percent of the patients were supported for more than 1 week, and 15% were supported for longer than 3 weeks.

The 57 patients came from 12 centers in the United States, from one center in England, and from European centers in association with the Cardiovascular Research Institute in Sion, Switzerland (12 patients).

Forty-six (81%) of the 57 patients underwent transplantation. Thirty-eight patients (83%) were discharged after orthotopic cardiac transplantation. The overall survival was 67% (see Table 4). The medical reasons for the 11 patients not qualifying for transplantation are listed in Table 9. Bleeding and multiorgan failure were the principal causes. The causes of death in the 8 patients (17%) who did not survive transplantation are listed in Table 10. They included graft failure, infection, multiorgan failure, rejection, and coagulopathy. Mortality was not affected by duration of pump support. The device-related complications are listed in Table 11. The bleeding complication resulted from hemorrhage in the left atrial appendage as the result of an attempt to insert a cannula in a patient who was too large for the length of the cannula. One patient who sustained a transient ischemic attack also had sepsis and eventually died. A transient ischemic attack occurred in 2 additional patients; in the first after the device had been off for 20 minutes, and in the second after the patient had received no anticoagulation therapy for 3 weeks. The two incidences of console dysfunction did not result in morbidity or mortality.

Table 5. Medical Causes of Not Performing Transplantation in 10 Patients With Novacor Device[a]

Cause	No. of Patients	Percentage
Multiorgan failure	3	33
Stroke (air, mural thrombus)	2	22
Hemorrhage (iatrogenic)	1	11
Respiratory failure	1	11
Loss of peripheral vascular tone	1	11
Acute rejection at implantation	1	11
Cardiovascular collapse in patient bridged for severe rejection	1	11

[a] Of these 10 patients, 9 have died and 1 is awaiting a donor.

Comment

Today prosthetic cardiac devices are being developed for three different clinical goals: cardiac support for eventual

Table 6. Device-Related Complications Among 17 Patients With Novacor Device

Complication	No. of Patients
Superficial percutaneous lead infection	2
Drainage tube infection	1
Stroke (air, mural thrombus)	2

Table 7. Summary of Data on 4 Patients With Thermedics Device

Variable	No.	Cause
No transplant procedure	1	Multiorgan failure
Death after transplantation	2	Graft failure; multiorgan failure
Device-related complications	0	. . .

recovery of the heart, bridging to transplantation, and permanent cardiac support or replacement. The various devices currently in use can have application in more than one of these areas.

In assessing the results of a procedure and a specific device in any one area, in this case bridging to transplantation, one must focus on the goal of the procedure and the definition of success. It is easy to become distracted and mix different goals with different procedures and devices. The worthiness of the procedure and the device for each goal must be addressed separately.

The goal of bridging to transplantation is to perform orthotopic heart transplantation on an eligible recipient in terminal heart failure who was supported by a univentricular or biventricular prosthetic ventricle during the period he or she was awaiting a donor heart. The definition of success is accomplishing the goal with a minimum of morbidity and mortality at feasible costs and returning the patient to a quality life.

If the survival in bridging to transplantation is not comparable to the survival in elective cardiac transplantation, the death of a patient who was bridged could also represent a wasted heart. Taking a learning curve into consideration, these early results indicate that this is not the case. The key to not wasting donor hearts will become a function of the specificity of patient selection. At the point of device implantation, it is not always possible to know if secondary organ dysfunction is reversible. A properly functioning support system, given time, will usually reverse secondary organ dysfunction.

Table 8. Summary of Data on 57 Patients With the Thoratec Heterotopic Prosthetic Ventricle

Variable	Value
Age (yr)	
Mean	41
Range	13–58
Sex (No.)	
Male	47 (82%)
Female	10 (18%)
Etiology (No.)	
Coronary artery disease	29 (51%)
Cardiomyopathy	28 (49%)
Support system (No.)	
Biventricular	45 (79%)
Univentricular	12 (21%)
Duration of support	
Mean (days)	8.5
Range (days)	1–74
>1 wk (No.)	17 (30%)
>3 wk (No.)	9 (16%)

Table 9. Medical Causes of Not Performing Transplantation in 11 Patients With Thoratec Device

Cause	No. of Patients
Bleeding	5
Coagulopathy	3
Surgical	2
Infection	1
Multiorgan failure	3
Aspiration	1
Renal failure	1

If a donor organ becomes available before organ recovery can occur or if there is no recovery, one is faced with a difficult choice: to proceed with transplantation in the face of secondary organ failure, which brings with it a higher risk for the ultimate failure of the transplant and a wasted donor heart, or to completely abandon hope of eventual recovery. Most surgeons, except in the presence of clear contraindications, have chosen to give the patient the benefit of the doubt and have proceeded with transplantation. This accounts for a number of the deaths after transplantation. With time, experience, and careful follow-up, specific contraindications at the time of transplantation will be clearer. In the meantime, a patient who has infection, major neurological impairment, a consumption coagulopathy, or dysfunction of two or more secondary organs should not undergo transplantation.

The risk of infection itself deserves special comment in assessing bridging to transplantation. In 1984, with the advent of better technology, researchers began the most recent series of studies on the feasibility of bridging to transplantation. The potential of infection as a limiting factor was foremost in the minds of the investigators. Some surgical approaches call for the native heart to be removed and replaced with prosthetic ventricles (eg, Jarvik orthotopic prosthetic ventricles). Others require the heart to be left in place (heterotopic) and the device to be implanted in the left side of the abdomen or chest (eg,

Table 10. Cause of Death After Transplantation in 8 Patients With Thoratec Device

Cause	No. of Patients
Infection	2
Multiorgan failure	1
Rejection	1
Graft failure	3
Coagulopathy	1

Table 11. Device-Related Complications Among Patients With Thoratec Device

Complication	No. of Patients
Phrenic nerve (recovered)	1
Surgical bleeding (atrial cannulation site)	2
Transient ischemic attack	3
Device off	1
No anticoagulation	1
Sepsis	1
Console dysfunction	2

Novacor or Thermedics) or brought out onto the abdominal wall (eg, Thoratec). Each approach presents different risks of infection.

The early experience indicates that the percutaneous cannulas or leads have not led to infection ascending into the mediastinum whether heterotopic or orthotopic implants were used. However, in a report by Griffith and associates [4], patients with orthotopically implanted devices have had a large number of blood-borne infections in the mediastinum. With heterotopically implanted devices, mediastinal infection has not been a prominent problem. The surgical explanation for this probably lies in the fact that with the orthotopic approach, the native heart is removed and replaced with a large, polymeric foreign body without a tissue-adhering surface in a large, relatively avascular space with a noncollapsible, bony structure anteriorly and posteriorly. This is an opportunity for multiple areas of dead space, areas in which fluid and blood collect to become a source of blood-borne infection. Leaving the native heart in the mediastinum appears to prevent mediastinitis and encourage normal wound healing.

More clinical experience must be gained and more investigations must be undertaken before any conclusive statement can be made. One thing appears to be certain: the apparent tissue compatibility of many polymeric materials may have to be modified and improved to safely implant these devices orthotopically in the mediastinum. Some modifications to the surgical implantation technique to avoid areas of dead space may also lead to improvements.

Graft failure at the time of cardiac transplantation in this series may appear to be more common than that in an elective cardiac transplantation population. There is, however, no statistical validation for this statement. At this time, it is merely an observation. There are no data to evaluate whether right or left heart graft failure is more common.

There are some explanations as to why graft failure might occur. Once a device is implanted, there is a certain urgency to find a donor heart. In this circumstance, one might accept a donor heart that was borderline and would not normally be used in an elective situation. One also might go a long distance to retrieve it; hence, there is a prolonged period of ischemia. The pulmonary vascular resistance also may change with a device in place. There are very few clinical data available in this area. In addition, the clinical urgency of device implantation may prevent a thorough evaluation of pulmonary vascular resistance before the device is implanted. When the device is implanted for technical reasons in a patient receiving biventricular support, it is difficult to monitor pulmonary vascular resistance over a prolonged period.

The need for biventricular heterotopic devices versus univentricular devices is not yet clear. Laboratory data on normal hearts indicate that a left-sided mechanical assist device does not adversely affect right ventricular function [5]. The pathophysiological events surrounding a clinical situation are quite different. Left univentricular assistance does not prevent ventricular arrhythmias, and its success commonly depends on right ventricular pharmacological support. The management of a patient after implantation is greatly simplified by the insertion of biventricular pumps. The difficult clinical decision occurs at the time of implantation, when one must decide on the need for a right ventricular pump. Pump selection is affected by this, as some heterotopic pumps can be used only on the left side (Novacor, Thermedics). More careful experience is necessary before this issue will be resolved. In the Thoratec experience with 57 patients, biventricular pumps were used 79% of the time. The decision to use biventricular pumps was a clinical judgment and was not based on precise hemodynamic guidelines, but these guidelines are being developed.

We are still early in the learning curve of clinical pump technology. The early results of bridging to transplantation have been very encouraging and have specifically demonstrated that the body and its organs can be very tolerant of an artificial pumping device that provides a cardiac output over prolonged periods. This is quite different from those devices being acceptable as permanent devices. Although the pumps on the whole have performed extraordinarily well, the next step involving permanent implantation of the energy systems will be challenging. In 1988, bridging to transplantation represents an important clinical proving ground for new pumps prior to their final permanent designs. In addition, it offers a valuable therapy for a limited number of patients.

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Current Status of Permanent Total Artificial Hearts

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Pneumatic total artificial hearts, although demonstrating utility as temporary mechanical circulatory support devices, have not demonstrated a great deal of promise as permanent cardiac replacements. The increasing number of patients who would be candidates for total heart replacement suggests a large role for a permanent implantable total artificial heart. To that end, the Pennsylvania State University is developing an electric motor–driven total artificial heart; the results with implants in calves are encouraging. In this device, a roller-screw mechanism is used to translate the rotation of a brushless direct-current motor into rectilinear motion of a pusher-plate assembly, which in turn empties the blood sacs. The total artificial heart of the future will function under automatic control without percutaneous leads, and this should provide the patient with a nearly normal life-style. Although further experimental efforts are necessary to prepare the device for clinical trials, the technology to provide a safe and reliable electric blood-pump system is at hand.

(Ann Thorac Surg 1989;47:172–8)

Pneumatically powered total artificial hearts (TAHs) have been employed as permanent devices in at least 5 patients, and as bridges to transplantation in more than 56 patients [1]. Complications with these devices, such as thromboembolism and infection, currently appear to be limiting factors in the application of the devices as permanent replacements. Although these complications exist when the devices are used as bridges to transplantation, the relatively short period of use reduces the risk to the patient.

Future TAH devices will be completely implantable, will have improved geometry and materials to reduce or eliminate thromboembolic complications, and, with no percutaneous leads, should produce fewer infectious complications. These future artificial hearts will be automatically controlled and provide the patient with a nearly normal life-style. The initial design of these future TAHs will provide for a design life of 5 years.

As of January 1, 1988, the National Heart, Lung, and Blood Institute of the National Institutes of Health began funding the development of these devices. The funding is in the form of contracts continuing through 1993. At that time, the devices should be ready to begin preclinical testing. Clinical application could begin by the year 2000.

Permanent Total Artificial Hearts

Four institutions are involved in this contract program: the Pennsylvania State University (Penn State), the University of Utah (Utah), Abiomed, Inc, and Nimbus, Inc. All are developing devices driven by electric motors. Of these four groups, two, Penn State and Utah, have employed their devices in vivo [2–4]. The longest surviving animal at Utah with their axial-flow pump-driven artificial heart is approximately 1 month [5]. Penn State has had 1 animal live for 222 days with an earlier design and 1 calf live 134 days with the current design.

The electric motor–driven TAH that has been utilized in animals at Penn State is shown in Figures 1 and 2. The blood pumps are constructed of an extremely smooth, seam-free polyurethane sac supported within rigid polycarbonate cases. Björk–Shiley monostrut valves are used at the inlet and outlet of each pump. The left and right blood pumps are alternately actuated by an assembly of two pusher plates situated, along with the motor drive, between the pumps. A roller-screw mechanism translates rotation of a brushless direct-screw motor into rectilinear motion of the pusher-plate assembly. Neodymium iron magnets and state-of-the-art winding techniques are used in the construction of the electric motor.

Also shown in Figure 1 is a compliance chamber, which is implanted in the thoracic cavity to compensate for changes in barometric pressure, differing stroke volumes between the left and right pumps, and diffusion of gases from the system. The infusion port attached opposite the compliance chamber is implanted subcutaneously and is utilized for sampling and replenishing gases. At the upper right in Figure 1 is the percutaneous lead used to test the device in animals without an implanted control system or energy source. A hermetic feed-through in this line seals the device from the outside, thereby allowing testing of the device, the compliance chamber, and the sampling port as they will be when the entire system is implanted.

This system has been implanted in 6 calves; the average survival is 46 days. The system has a stroke volume of 100 mL and a maximum output of 12 L/min. Animals typically weighed 100 kg at implantation. As they gain about 0.5 kg per day, the animals quickly outgrow the device. Future systems for clinical use will have a 70-mL displacement and will undergo in vivo testing in mature sheep.

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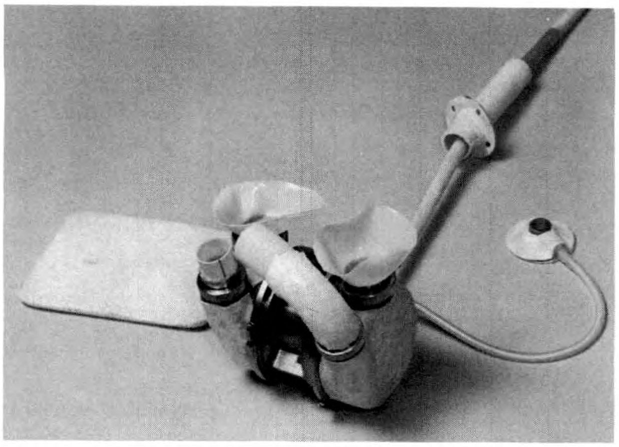


Fig 1. The assembled electric motor total artificial heart system. Gas displaced from the motor during a cardiac cycle is held in the compliance chamber (left), which acts as a reservoir. The compliance chamber volume can be checked by using the sampling port (right). Atrial cuffs and vascular grafts are sewn to the native structures; union nut connectors allow the device to then be easily attached.

Future Devices

The 70-mL nominal stroke volume device being developed at Penn State operates on the same principle, with the same mechanism, as the 100-mL device that has been tested in calves. The new system employs a smaller electric motor drive, with pumps having reduced diameters and requiring smaller pusher-plate excursions for full ejection. The system is intended to be used in humans as shown in Figure 3. The device is implanted intrathoracically along with the compliance chamber. The infusion port is placed subcutaneously over the ribs. Implanted in the preperitoneal space are the electronic devices necessary to power and control the artificial heart.

In this new artificial heart, we will make use of new materials as they become available. New permanent magnet materials and less-resistive conductors (or possibly superconductors) will raise motor efficiency. New ceramics, hybrid steel-ceramics, or ion-implanted steel parts for the mechanism will provide longer life and improved efficiency. New polymers and improved manufacturing techniques will provide better blood-contacting surfaces. Pump cases, motor housings, and selected internal components may be constructed of composites such as those based on boron, Kevlar, or carbon fibers. By combining new materials with proven design principles, we intend to produce a smaller, lighter device that has improved efficiency and a life expectancy exceeding 10 years.

Electronic Control

Current Methods

Maintenance of left atrial pressure (LAP) within a physiological range is central to effective control of a TAH. In the natural heart, LAP is the result of a balance between the Starling sensitivities of the left and right ventricles. With a given hormonal and neural background, a given right atrial pressure will give rise to a corresponding right cardiac output. On the average, the left heart provides a cardiac output (CO) equal to the right cardiac output plus the bronchial flow. Depending on the left heart sensitivity, this requires a certain LAP. Our TAH operates in a similar fashion in that LAP is the result of the characteristics of the ventricles. We do not control LAP directly in the sense of holding it to a preset value.

The control system analyzes the energy demand of the electric motor and determines for each pump cycle the extent of fill of the left pump. This information is averaged, typically over five beats, to provide a measure of average left pump stroke volume. If left pump stroke volume begins to fall, left systole is made longer. Because left systole occurs during right diastole in the alternately ejecting system, the right pump is given more time to fill and increases its stroke volume, and LAP rises, thereby correcting the deficit in left pump filling. As the left pump begins to fill consistently, left systole is made more rapid,

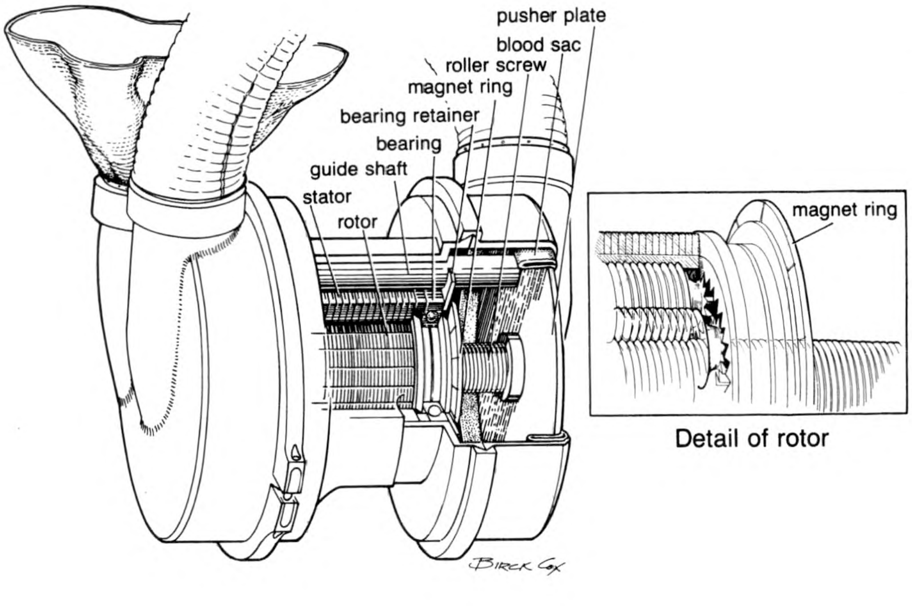
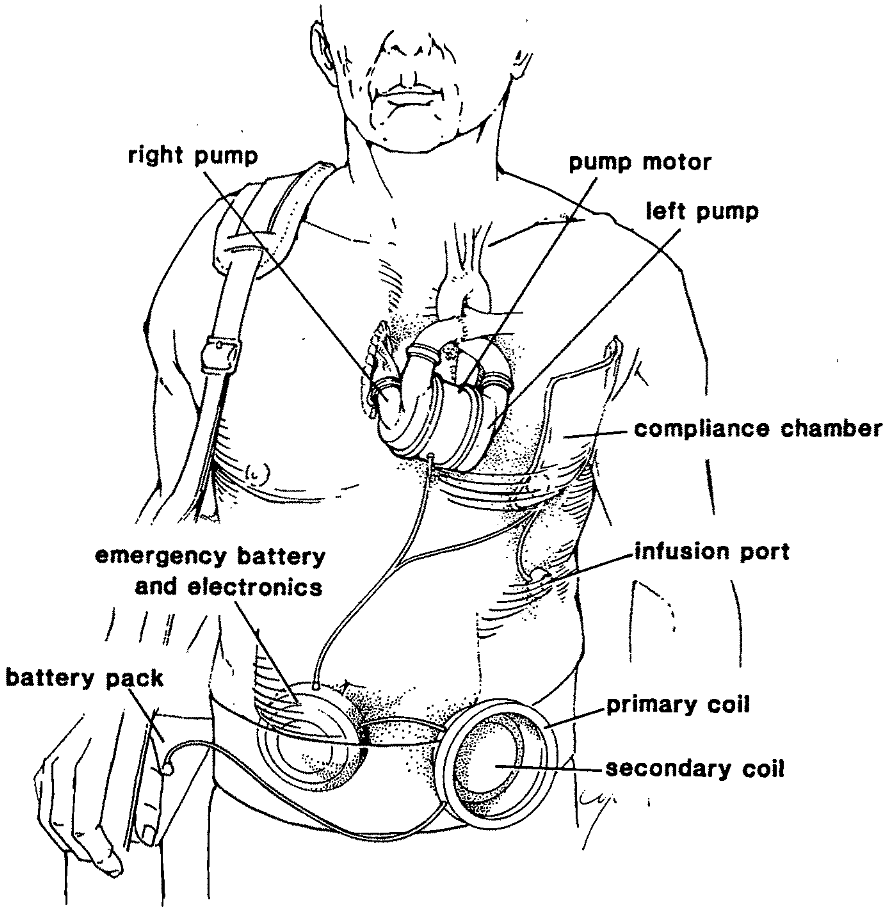


Fig 2. The makeup of the roller-screw mechanism. This mechanism translates rotation of a brushless direct-current motor into rectilinear motion of the pusher-plate assembly, which then ejects blood from the blood sac. Reprinted with permission from: Rosenberg G, Pierce WS, Snyder AJ, Weiss W, Landis D, Pae W, Magovern J. In vivo testing of a roller-screw type electric total artificial heart. In: Unger F, ed. Assisted Circulation 3. New York: Springer Verlag, in press.

Fig 3. The system as it will appear in clinical use. The light battery pack gives the patient complete mobility. Reprinted with permission from: Rosenberg G, Pierce WS, Snyder AJ, Weiss W, Landis D, Pae W, Magovern J. In vivo testing of a roller-screw type electric total artificial heart. In: Unger F, ed. Assisted Circulation 3. New York: Springer Verlag, in press.



shortening right diastole, reducing right pump stroke volume, and causing a fall in LAP.

In practice, a stable point is reached at which the left pump just barely fills on the typical beat. The left pump operates at a lower volumetric efficiency than does the right because of the higher backflow losses of the tilting-disk valves at systemic pressures. The left pump must also supply bronchial circulation, which returns to it directly. Therefore the stable point is characterized by incomplete filling of the right pump.

From a stable point, suppose there is a rise in right atrial pressure. The right pump will fill more completely, its output will rise, and LAP will rise. The resultant increase in the rate of fill of the left pump will be detected by the controller, and left systole will be made increasingly more rapid until LAP is stabilized. Because left systole has been made shorter and no other timing changes have been made, the beat rate has risen. The left pump is still filling completely, and therefore CO has risen. The LAP is now stable at the level necessary to support the higher CO. Our method of maintaining stable LAP has given rise to classic "Starling" behavior in the TAH.

We can augment or suppress this behavior according to the manner in which we manipulate the speed of left diastole. If left diastole is made shorter when left systole is shortened, the slope of the CO curve is made steeper. We have achieved sensitivity similar to that exhibited by the textbook Starling preparation in vitro. If left diastole is made longer when left systole is made shorter, we can suppress sensitivity of CO to right atrial pressure, and apply control over CO according to afterload, as our group [6] has done with the pneumatic TAH.

Future Directions

The Starling preparation behavior we have demonstrated seems extremely useful and appears to be a reasonable approximation of the function of a transplanted heart. The afterload-derived control has worked well for our group. Either of these means of controlling CO, or even a constant CO, is acceptable. Indeed, in patients who have received a pneumatic TAH and have regained some level of activity, the lack of a crisply responding control over CO does not seem to have been a serious problem.

Both of these techniques, however, have shortcomings. Animals with artificial hearts appear to exhibit a pathological condition in their regulation of extracellular volume, a condition characterized by rising central venous pressure reminiscent of congestive heart failure, despite adequate CO. Patients receiving a TAH have, at times, required treatment with substantial doses of diuretics despite adequate CO and apparently normal renal function. This pathological condition may be related to removal of atrial natriuretic peptide–secreting atrial tissues, but this is unproven [7]. In the meantime, right atrial pressure remains a control signal of questionable utility.

Cardiac output control based on afterload is intended to

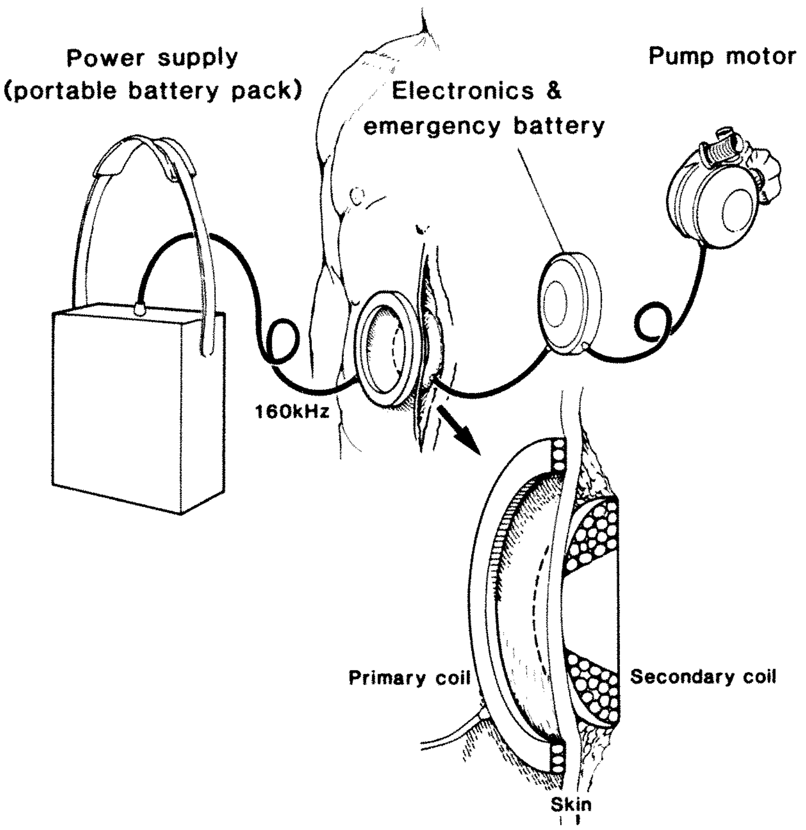


Fig 4. The transcutaneous energy transmission system. The primary and secondary coils allow energy to be passed without the need for percutaneous lines. Reprinted with permission from: Rosenberg G, Pierce WS, Snyder AJ, Weiss W, Landis D, Pae W, Magovern J. In vivo testing of a roller-screw type electric total artificial heart. In: Unger F, ed. Assisted Circulation 3. New York: Springer Verlag, in press.

respond to bodily demand as reflected in autoregulatory changes in peripheral resistance. In practice, peripheral resistance is the result of a composite of tissue demand and other factors, and therefore is a completely reliable signal only if the other factors remain constant.

These shortcomings are the direct result of the fact that we are indeed working with an isolated heart. The natural heart in situ is not isolated, ie, is not a Starling preparation. We have shown that it is possible for an artificial heart to mimic the natural heart's response to the hemodynamic state. We have not yet developed a TAH responsive to the recipient's neural or biochemical state.

Means for detecting biochemical signals may become available in the form of chemically sensitive field-effect transistors for direct measurement of blood or tissue chemistries, and optical sensors for measurement of blood oxygen saturation and hematocrit [8]. These devices promise to make available signals that indicate the sufficiency of CO, especially in the otherwise healthy patient who has normal electrolytes and no respiratory insufficiency. Care must be taken in making use of signals such as arterial oxygen saturation, which is normal even in the hyperperfused patient and departs from normal only when CO becomes insufficient. Measures such as arterial-venous oxygen difference or venous carbon dioxide may be more appropriate.

In any case, the anticipatory characteristic of the nervous system may be difficult to duplicate, and direct neural connections may be required to come close to duplicating the response of the natural heart to the whole-body state. Techniques will need to be developed to place the required chronic sensors and to process the signals properly.

Energy Transmission

The ability to efficiently transmit a sufficient amount of electrical energy (10 to 20 W) across intact skin with reasonable cosmetics and simple implantation has been well established. The best-known technique was proposed by Schuder and co-workers [9] and later developed into a usable device by Sherman and colleagues [10]. The device of the latter group has been shown to operate well in vivo. The implanted and overlying external coils through which energy is inductively transmitted are shown in situ in Figure 3 and in greater detail in Figure 4.

While continuing to apply the basic principles set down by Schuder and colleagues [9], we have set out to design a second-generation energy and information transmission system. This device will maintain good efficiency (nominally 80%) over a wide power range while simultaneously supporting bidirectional transmission of information. Once simultaneous information transmission is achieved, a monitoring device contained in the patient's battery pack can query the implanted controller for any desired information. Although it is important to avoid burdening the patient with information about the function of the device, it is important that knowledge not be lost by failing to collect available data. The information link can also be used to adjust the controller itself. This is especially important in the early period after implantation.

Power Sources

Like an electric automobile, an electric artificial heart must be designed with the limitations of available power sources in mind. Current battery technology dictates that we assemble battery packs from nickel-cadmium cells. Nickel-cadmium batteries must be treated in certain ways to perform effectively, especially in terms of cycle life. This is especially important for the implanted pack because it cannot be replaced easily. This problem is also a consideration for the external pack, as its failure cannot be classified as an inconsequential event for the patient.

Specifically, nickel-cadmium cells must be discharged completely, at least occasionally, if they are to retain their full capacity. This requirement stems from the so-called memory effect, which is the tendency of these cells, after repeated partial discharges, to refuse to supply more energy than has been previously drawn from them. A patient who habitually uses a pack for half its rated time may eventually find that it fails if he or she then tries to use it for a longer period.

For the primary (external) power source, this problem can be avoided by keeping three or more packs in rotation, each rated at half the required energy (eg, five-hour packs for ten-hour operation). At a given time, the patient wears two of the packs while one or more others recharge. The system draws energy from one pack until it is completely discharged, and then switches to the second pack while the first is replaced and put on a separate charger. Energy continues to be drawn from the second pack until the third is needed, and so on. The patient can rotate packs indefinitely, "plugging in" to a nonportable power source only to sleep. Treatment of the packs is placed largely in the hands of the device designer. The packs are recharged by a separate console, which can perform evaluations necessary to identify and reject any pack that is soon to fail.

It is quite likely that, within 5 to 10 years, cells based on lithium chemistry will be made sufficiently reliable and safe to be used in these devices. Lithium chemistry has the advantage of a substantial reduction in size and a small reduction in weight over nickel-cadmium chemistry. In addition, the first rechargeable lithium cells are free from memory effects. Rather, they perform best and provide the greatest number of cycles before failing if they are discharged only partially most of the time. This kind of cell behavior is consistent with reasonable human behavior regarding use of the implanted battery: the pack will last longer if the patient takes a conservative approach to its use.

Device Implantation

Patient preparation and exposure for implantation of the electrically driven TAH will be similar to the techniques utilized for orthotopic cardiac transplantation. A median sternotomy is made, and the patient is placed on cardiopulmonary bypass with individual cannulation of both the superior and inferior vena cava for venous return to the bypass circuit. It is important to place the caval cannulas as close to the caval–atrial junction as possible, leaving the free wall of the right atrium untethered. Arterial cannulation is most often performed in the ascending aorta unless the patient has a small chest size or short ascending aorta. In such cases, femoral cannulation may be preferable.

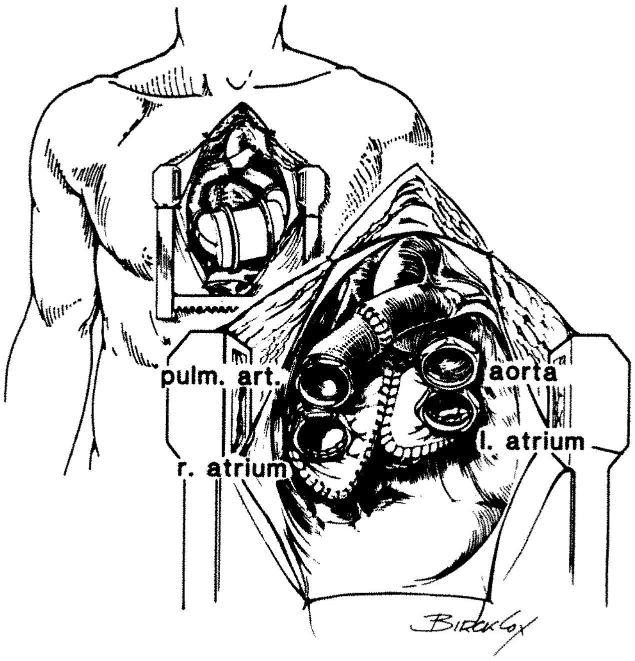


Fig 5. The clinical situation just prior to the attachment of the device. The atrial and vascular grafts have been sewn to the corresponding native structure. (l. = left; pulm. art. *= pulmonary artery;* r. *= right.)*

Caval tapes are tightened, and the aorta is crossclamped. The native heart is excised by dividing the atria along the atrioventricular groove, and the great vessels are divided above their respective semilunar valves. Implantation of the device is greatly facilitated by preserving as much atria and as much great vessel length as possible. Atrial cuffs made of polymer-coated fabric are sewn to the native atria, and Dacron vascular grafts are sewn to the aorta and the pulmonary artery (Fig 5). All four grafts have attached union nut connectors, which allow rapid attachment of the electric pump.

After the left atrial, pulmonary artery, aortic, and right atrial grafts are sewn into place using two suture lines of running 3-0 polypropylene, each anastomosis is tested for leaks. This procedure is critical, as it is very difficult to see the suture lines once the device is in place. Leak testing is performed using an occlusive threaded cap connected to an intravenous bag of methylene blue–stained crystalloid solution. Once the occlusive cap is connected to the union nut connector of the graft being tested, the intravenous bag is elevated to distend the anastomotic line and leaks thus identified are oversewn with pledgeted sutures.

Often it is difficult to obtain appropriate positioning of the right atrial graft to provide optimum orientation of the device. It is helpful to use a template of the left and right atrial connectors on the electric heart as a guide to situating the right atrial anastomosis. This template can be periodically placed in the chest during placement of the grafts to ensure that the ultimate position of the device is correct.

The electric motor artificial heart is then brought to the field and, starting with the left atrium, is connected to the grafts using the attached union nut connectors. If there is difficulty in placing the device in the recipient's chest using standard techniques, it may be necessary to remove the pericardium anterior to the phrenic nerve to allow the device to be oriented to the left hemithorax. After the electric heart is connected and in place, the air must be removed before the initiation of pumping. This procedure is performed using small catheters that are inserted into the blood sacs through the atrial suture lines to aspirate any air present.

The compliance chamber is situated in the left chest with the sampling port tunneled to lie subcutaneously in a pocket created in the left upper quadrant (see Fig 3). The pump's electrical driveline is then passed subcutaneously to the periumbilical area where it is connected to the emergency battery and electronics package, which lie in a subcutaneous pocket at the approximate level of the belt line. The primary coil for the transcutaneous energy system is situated in a similar fashion just to the patient's left of the implanted electronics and emergency battery.

Pumping is then initiated, ventilation is resumed, and the patient is weaned from cardiopulmonary bypass. All suture lines are carefully examined to ensure hemostasis. The cannulas are removed in the usual fashion, mediastinal drainage tubes are placed, and the sternotomy is closed routinely.

Life-Style Considerations

It is naive to think that we will have, within a few years, a device that will support a patient's entire circulation while he forgets its existence in his chest entirely for long periods of time. Rather, current technology, especially relating to power sources, will require that the device receive a modest amount of care from the patient. We believe, however, that we are on a path to developing a device that a patient can forget to the degree one forgets peritoneal dialysis, insulin injections, or colostomy devices. Although periodic attention will be absolutely necessary, constant attention will not be required.

Generally, attention to the device will consist of changing the external battery and planning ahead for continued availability of power. Ordinarily the externally worn package will signal only the need to align energy transmission coils or change a battery. This device will not continuously generate any signal indicating its operational state.

The means of dealing with unusual conditions must be determined with great care. Clearly, it is crucial that detection of abnormal operation triggers a call for professional attention. False alarms, however, or alarms due to problems of little real consequence can seriously erode patient confidence. Limitations on life-style would follow. The more reliable the device is made through careful design and manufacture, the less difficult this issue becomes. One does not monitor a pacemaker daily because pacemakers rarely fail.

We must still deal with failure of judgment or inattention on the part of the patient. Misalignment of energy transmission coils will be signaled audibly, gently at first and then with greater volume. If the patient remains disconnected from external power too long, CO will begin to be limited to conserve the remaining energy. This kind of operation can serve to make excessive time away from a constant power source feel similar to excessive aerobic activity. If carefully implemented, such operation could discourage inappropriate inattention while actually helping the patient feel the ties between the device and himself.

Patient Care

Medical Care

The immediate postoperative care of the patient will be similar to that given to a patient undergoing a routine cardiac operation. When appropriate, the patient is weaned from the ventilator, the mediastinal drainage tubes are removed, and the patient is transferred from the intensive care unit. After recovery from the operative experience, the patient may be discharged home with healing wounds. The recipient should be maintained on long-term anticoagulation with orally administered warfarin sodium to help prevent thromboembolic complications. Prothrombin time should be maintained at approximately two times normal in the usual fashion.

Careful attention to anticoagulation, wound healing, and mechanical function demands routine clinic visits, especially in the first several months after operation. During these visits, a complete physical examination should be performed; evidence of left or right ventricular failure or embolic complication should be sought. Evaluation of mechanical function can be performed in conjunction with the engineering staff at the same time.

It is important to remember that these patients are prone to device-related infectious complications. Even transient bacteremia can lead to a devastating complication. Although long-term antibiotic therapy is not recommended, antibiotic coverage for procedures or problems associated with bacteremia is suggested.

Care of the Device

The device is designed to operate over its full lifetime without scheduled service or intervention of any kind. Care will consist only of careful monitoring of device operation, both as the designer sees it (eg, power consumption at a given flow and pressure) and as the patient sees it (eg, the general degree of comfort with various aspects of living with the device). The device and all of its components are to be engineered so that they reliably provide a given duration of service. We cannot guarantee, however, that normal wearing out of a device will be the limiting factor in a patient's lifetime, or that unforeseeable failures will not occur. Clearly, investigators should be prepared to replace a device or component (eg, a battery) that is failing if such a situation arises.

Summary and Conclusions

Although clinical experience has demonstrated that pneumatically powered artificial hearts can be used successfully for temporary circulatory support, attempts at "permanent" use of these devices have been less promising [1]. The large number of patients with biventricular failure as well as the limited number of cardiac allografts available suggests a large role for the permanently implantable TAH.

At the Pennsylvania State University, work is in progress on an electric motor–driven TAH employing a roller-screw motion translator. Initial experimental experience with this system in the calf model has been encouraging, with survival of as long as 134 days. The development of an adult model, such as mature sheep, may be helpful in eliminating the problem of recipient growth as well as blood sac calcification seen in implants in calves.

Remarkable improvements have occurred in the development of implantable blood pumps, and we expect to incorporate advances in related fields as they become available. Advances in microprocessors, the weight of structural components, permanent magnet materials, and low-resistance conductors all have roles to play in the evolution of a reliable totally implantable artificial heart. As it stands now, the technology exists to implant an electric blood-pump system that should provide a reasonable life-style and function reliably with minimal care. Only further cooperative experimental efforts will provide the answers necessary to make this device ready for clinical implantation.

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THE
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Official Journal of The Society of Thoracic Surgeons
and the Southern Thoracic Surgical Association

EVENTS OF INTEREST

Brief notices of meetings, courses, and symposia relevant to cardiothoracic surgery are published as a service. They should be formatted as follows: meeting title, date, place, sponsor, accreditation, director, fee, minimum/maximum attendance, and address/phone for further information.

Announcements should be sent at least 4 months in advance of publication to *The Annals of Thoracic Surgery*, 3108 Queeny Tower, Barnes Hospital Plaza, St. Louis, MO 63110-1041; phone, (314) 361-6084.

Pathophysiology and Techniques of Cardiopulmonary Bypass: IX, San Diego, California—February 16–19, 1989

This symposium is sponsored by the Cardiothoracic Research and Education Foundation. The symposium is accredited for 17 hours in category 1 for the Physician's Recognition Award of the AMA. The American Board of Cardiovascular Perfusion has alloted 30 recertification points to perfusionists in attendance, and the symposium is approved by the American Association of Nurse Anesthetists for 17 CE credits and by the California BRN for 17 hours of nursing credit. For information, contact the Cardiothoracic Research and Education Foundation, PO Box 33185, San Diego, CA 92103.

Thoracic Organ Transplantation, Tucson, Arizona—February 23–25, 1989

This conference is sponsored by Abbott Northwestern Hospital, and is accredited for 13 hours in category 1 of the Physician's Recognition Award of the AMA. For information, contact the Minneapolis Heart Institute Foundation, Education Services, Suite 60, 920 East 28th St, Minneapolis, MN 55407; or telephone (800) 328-5015.

Critical Care in the 1990s, Aruba—April 22–28, 1989

For information on this meeting, contact Omar Prakash, MD, Thorax Centre, Erasmus University, PO Box 1738, 3000 DR Rotterdam, the Netherlands; or telephone 31-10-4635230 (telex: 25267; facsimile: 31-10-4362841).

International Society for Heart Transplantation, Munich, Federal Republic of Germany—April 23–25, 1989

For information on this meeting, contact the Headquarters Office, 435 North Michigan Ave, Suite 1717, Chicago, IL 60611; or telephone (312) 644-0828.

Sixty-ninth Annual Meeting of The American Association for Thoracic Surgery, Boston, Massachusetts—May 8–10, 1989

For information on this meeting, contact AATS, 13 Elm St, Manchester, MA 01944; or telephone (508) 526-8330.

Vascular Surgery 1989, New York, New York—May 18–20, 1989

This symposium is cosponsored by the Long Island Vascular Clinic; the Long Island Jewish Medical Center; and the Postgraduate Institute for Medical and Dental Education, the Health Sciences Center, and the School of Medicine, State University of New York at Stony Brook. The symposium is accredited for 24 hours in category 1 from the Accreditation Council for Continuing Medical Education and the AMA. For information, contact Ann J. Boehme, CMP, Associate Director for Continuing Education, Long Island Jewish Medical Center, New Hyde Park, NY 11042; or telephone (718) 470-8650.

First International Symposium on Heart Failure: Mechanisms and Management, Jerusalem, Israel—May 21–25, 1989

This meeting is sponsored by the Israel Heart Society. For information, contact the Secretariat, First International Symposium on Heart Failure, PO Box 50006, Tel Aviv 61500, Israel; or telephone (03) 654571 (telex: 341171 KENS IL; facsimile; 972-3-655674).

Heart Surgery 1989: Third International Symposium on Cardiac Surgery, Rome, Italy—May 29–June 2, 1989

For information on this meeting, contact the Organizing Secretariat, Assistenza Internazionale Servizi di Congresso, Viale Parioli 2, Rome 00197, Italy.

General Thoracic Surgery, Toronto, Canada—June 1–2, 1989

For information on this meeting, contact Continuing Education, Faculty of Medicine, Medical Sciences Building, University of Toronto, Toronto, Ontario, M5S 1A8, Canada; or telephone (416) 978-2718.

Eighteenth Annual Society of Critical Care Medicine Educational and Scientific Symposium, New Orleans, Louisiana—June 5–9, 1989

For information on this meeting, contact the Society of Critical Care Medicine, 251 East Imperial Highway, Suite 480, Fullerton, CA 92635; or call (714) 870-5243.

International Symposium on Surgery for Heart Valve Disease, London, United Kingdom—June 12–16, 1989

This symposium is sponsored by Baxter Edwards CVS Division, Carbomedics, Medtronic, Pergamon Press, Inc, Shiley, St. Jude, and USCI International, and will focus on material and designs of replacement heart valves. The symposium is accredited for up to 30 hours of category 1 of the Physician's Recognition Award of the AMA. For information, contact the Symposium Secretariat, Conference Associates HVD, Congress House, 55 New Cavendish St, London W1M 7RE, United Kingdom; or telephone 01-486-0531 (telex: 934346 CONFAS G; facsimile: 01-935-7559).

International Society for Cardiovascular Surgery/Society of Vascular Surgeons, New York, New York—June 18–21, 1989

For information on this meeeting, contact the Association offices, 13 Elm St, Manchester, MA 01944; or telephone (508) 526-8330.

Western Thoracic Surgical Association, Monterey, California—June 21–25, 1989

For information on this meeting, contact the Association offices, 13 Elm St, Manchester, MA 01944; or telephone (508) 526-8330.

Third Annual Meeting of the European Society for Vascular Surgery, Malmö, Sweden—September 3–5, 1989

A satellite symposium on pharmacological intervention to increase patency in arterial reconstructions will be held in the same location on September 6–7, 1989. For information on both symposia, contact the Congress Organisation Bureau, ESVS 89, c/o ICM AB, Geijersgatan 50, S-216 19 Malmö, Sweden.

Fourth World Congress of the International Society for Diseases of the Esophagus, Chicago, Illinois—September 6–8, 1989

This meeting is sponsored by the American College of Chest Physicians and Smith Kline & French Laboratories and is accredited for hour-to-hour credit in category 1 of the Physician's Recognition Award of the AMA. For information, contact the American College of Chest Physicians, PO Box 93826, Chicago, IL 60673.

Twenty-fifth Annual Meeting of The Society of Thoracic Surgeons, Baltimore, Maryland—September 10–13, 1989

For information on this meeting, contact George C. Kaiser, MD, The Society of Thoracic Surgeons, 111 East Wacker Dr, Chicago, IL 60601-4301.

Thirty-eighth Annual Meeting of The Scandanavian Association for Thoracic and Cardiovascular Surgery and The Scandanavian Society for Extracorporeal Technology, Aarhus, Denmark—September 13–16, 1989

For information on this meeting, contact the Secretary of the Congress Committee SATCVS/SCANSECT, Chr. Mouritzen, MD, Department of Thoracic and Cardiovascular Surgery, Skejby Sygehus-Aarhus University Hospital, DK-8200 Aarhus N, Denmark.

National Conference on Pediatric Trauma, Ann Arbor, Michigan—September 20–23, 1989

This meeting is sponsored by the University of Michigan Medical School, the Kiwanis Pediatric Trauma Institute, and the New England Medical Center. The meeting is accredited for 20 hours in category 1 of the Physician's Recognition Award of the AMA. For information contact Debbie DeSmyther, Program Assistant, Office of Continuing Medical Education, Towsley Center-Box 0201, University of Michigan Medical School, Ann Arbor, MI 48109-0201; or telephone (313) 763-1400.

Thirty-sixth Annual Meeting of the Southern Thoracic Surgical Association, Phoenix, Arizona—November 9–11, 1989

For information on this meeting, contact Gordon F. Murray, MD, Southern Thoracic Surgical Association, 111 East Wacker Dr, Chicago, IL 60601-4301.

1989 Anniversary Meeting of The Society of Thoracic Surgeons

The Twenty-fifth Anniversary Meeting of The Society of Thoracic Surgeons will be held at the Baltimore Convention Center in Baltimore, Maryland, September 11–13, 1989.

APPLICATION FOR MEMBERSHIP

(Deadline: May 1, 1989)

Requests for application forms for membership in The Society of Thoracic Surgeons should be addressed to Charles D. Campbell, MD, Chairman, Membership Committee, The Society of Thoracic Surgeons, 111 E Wacker Dr, Chicago, IL 60601.

The completed application forms and supporting letters must be in the hands of the Membership Committee by **May 1, 1989,** for the applicant to be considered for election at the meeting next September.

CALL FOR ABSTRACTS

(Deadline: February 15, 1989)

Abstracts for papers to be presented at the 1989 Anniversary Meeting are now being accepted. An original and 10 copies should be submitted, using the official Society abstract form (on verso of this page), to Fred A. Crawford, Jr, MD, and Gordon F. Murray, MD, Co-Chairmen, Program Committee (Abstracts), The Society of Thoracic Surgeons, 111 E Wacker Dr, Chicago, IL 60601. Additional forms are available upon request from The Society. Abstracts must summarize an original contribution not presented or accepted for presentation elsewhere. Abstracts must be in the hands of the Program Committee by **February 15, 1989.** Abstracts received after the deadline will not be considered. It is requested that the covering letter indicate the author who is to receive notice of acceptance or rejection and the author who will present the paper.

In addition to the regular program, there will be one-hour Research Forums on Tuesday and Wednesday mornings at the same time as the early morning breakfast sessions. Abstracts may be submitted for the regular Scientific Session or Research Forum. Papers selected for the Research Forum will be published in *The Annals* if they pass the usual editorial review.

Essayists are reminded that according to the bylaws of The Society, all papers accepted for presentation: (1) must be submitted in *triplicate* to the Secretary at the time of presentation or to the Editor of *The Annals of Thoracic Surgery* prior to presentation; and (2) become the property of The Society if they are accepted for presentation.

It is well recognized that abstracts frequently belie their content by virtue of poor organization, and as a result valuable contributions to the Scientific Sessions may be unrecognized. It is important that methods and results be clearly defined in the abstract; therefore, general statements such as "results will be presented" are not acceptable. When a procedure or method is stated to have "advantages," those advantages should be defined. Abstracts that simply summarize results without defining objectives and methods are equally undesirable.

Speakers for accepted papers are limited to ten minutes.

Instructions for Abstracts

The official abstract form, printed on verso of this page and available from The Society, or photocopies thereof, must be used. **Authors must indicate whether they want the abstract considered for the regular Scientific Session or the Research Forum by checking the appropriate box. Authors must also categorize the principal subject of their abstract by checking the appropriate box.**

1. Full names of authors must appear on the abstract.
2. Institution or address is to be given, but omit titles, degrees, and appointments.
3. Abstracts must be limited to 250 words and must be typed double-spaced.
4. When percentages are used, the absolute numbers of derivation must be stated.
5. The body of the abstract should include:
    a. A brief statement of the purpose of the study being presented, with reference to the current state of research in the field.
    b. The methods of study or experimental approach clearly, but briefly, defined.
    c. A summary of the results and/or conclusions of the study, including sufficient details to support those conclusions.
    d. A statement concerning the significance of the work and its possible implications for further research.
6. The form must be signed by the senior author attesting that the material will not be presented elsewhere if accepted for the scientific program nor published elsewhere if accepted for publication in *The Annals of Thoracic Surgery.*

In discussion of papers, The Society encourages a healthy spirit of constructive critical review and rebuttal by comments pertinent to the content of the paper being presented. Presentation of discussion in the form of "secondary papers" will not be welcomed.

CALL FOR SURGICAL FILMS OR VIDEO TAPES

(Deadline: February 15, 1989)

The popular surgical movie program will again be presented at the Baltimore meeting. The Program Committee hereby solicits the submission of surgical films, which may portray a surgical procedure or simply a technical maneuver that the surgeon thinks will be of interest to The Society. The film may not exceed ten minutes in length. Sound movies are acceptable but not necessary; however, live narration by the principal surgeon is a requirement for participation in the movie night program. The movies should be on 16-mm film or ¾-inch U-Matic video tape. The deadline for submission is **February 15, 1989.** Films and video tapes also should be sent to Fred A. Crawford, Jr, MD, and Gordon F. Murray, MD, Co-Chairmen, Program Committee, at The Society of Thoracic Surgeons, 111 E Wacker Dr, Chicago, IL 60601.

George C. Kaiser, MD
Secretary

For Committee use only:

THE SOCIETY OF THORACIC SURGEONS

Abstract Form

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Please forward curriculum vitae and three letters of recommendation to Jorge A. Wernly, MD, Chief, Division of Thoracic and Cardiovascular Surgery, University of New Mexico Medical Center, Albuquerque, NM 87131. An affirmative action/equal opportunity employer.

Cardiothoracic surgeon, BE/BC, wanted to join surgeon developing new program scheduled to begin spring 1989 in major southeastern city. Practice will include adult cardiac, thoracic, and peripheral vascular surgery. Will consider experienced individuals or those completing training June 1989. Salary and partnership negotiable. Please send curriculum vitae and recent photograph.

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2-Man thoracic and cardiovascular surgery group in the Southeast looking for new associate to do thoracic, cardiac, and vascular surgery. Must be board eligible or board certified in thoracic and cardiovascular surgery and have completed training in the recent past or by July 1, 1989.

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Cardiac surgeon sought for beautiful Rocky Mountain region. 200+ cases per year in a 282-bed regional hospital. Excellent salary and benefits with bonus incentives leading to partnership after the third year. Outdoor activities abound in excellent living environment. Board certified/eligible required. Please respond with curriculum vitae and references.

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Cardiovascular and thoracic surgeon wishes to relocate. University trained with ABTS certification. Ten years experience with extensive cardiac, thoracic, and peripheral vascular surgery. Would be interested in starting new program or association with group. Curriculum vitae and references available upon request.

Please respond to W-539, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiovascular and thoracic surgeon, 37, ABS/ABTS certified, personable, excellent surgical skills and record, interested in opening new program or joining established practice.

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Cardiovascular and thoracic surgeon, 34, recent graduate, ABS certified, ABTS eligible. Additional year of experience in all aspects of cardiac surgery. Wishes to join an active cardiothoracic practice. Curriculum vitae, operative experience, and references available upon request.

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Please respond to W-550, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Mature board certified thoracic surgeon wishes to perform noncardiac thoracic surgery and/or function as surgical assistant with cardiothoracic group. New York City, either coast, or large metropolitan area preferred. CV and references on request.

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Cardiovascular and thoracic surgeon, 42, American, ABS, ABTS, ABVS. Eight years private practice experience. Completing overseas fellowship in heart and heart/lung transplantation July 1989. Seeks opportunity with program involved in transplant surgery. Curriculum vitae and references upon request.

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Cardiovascular and thoracic surgeon, mid-50's. University trained, ABS/ABTS, 14 years of extensive and highly successful solo practice in vein and IMA CABG, valve, pulmonary and vascular surgery. Experienced in starting open heart program. Strong surgical and clinical skills. Seeking private practice opportunity, either starting new program or in association with established individual or group.

Please respond to W-100, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiovascular and thoracic surgeon, 40, wishes to relocate, preferably in the Southeast. American university trained, ABS, ABTS, FACS. Private practice experience in adult cardiac, thoracic, and peripheral vascular surgery. Willing to initiate new program. Curriculum vitae and references upon request.

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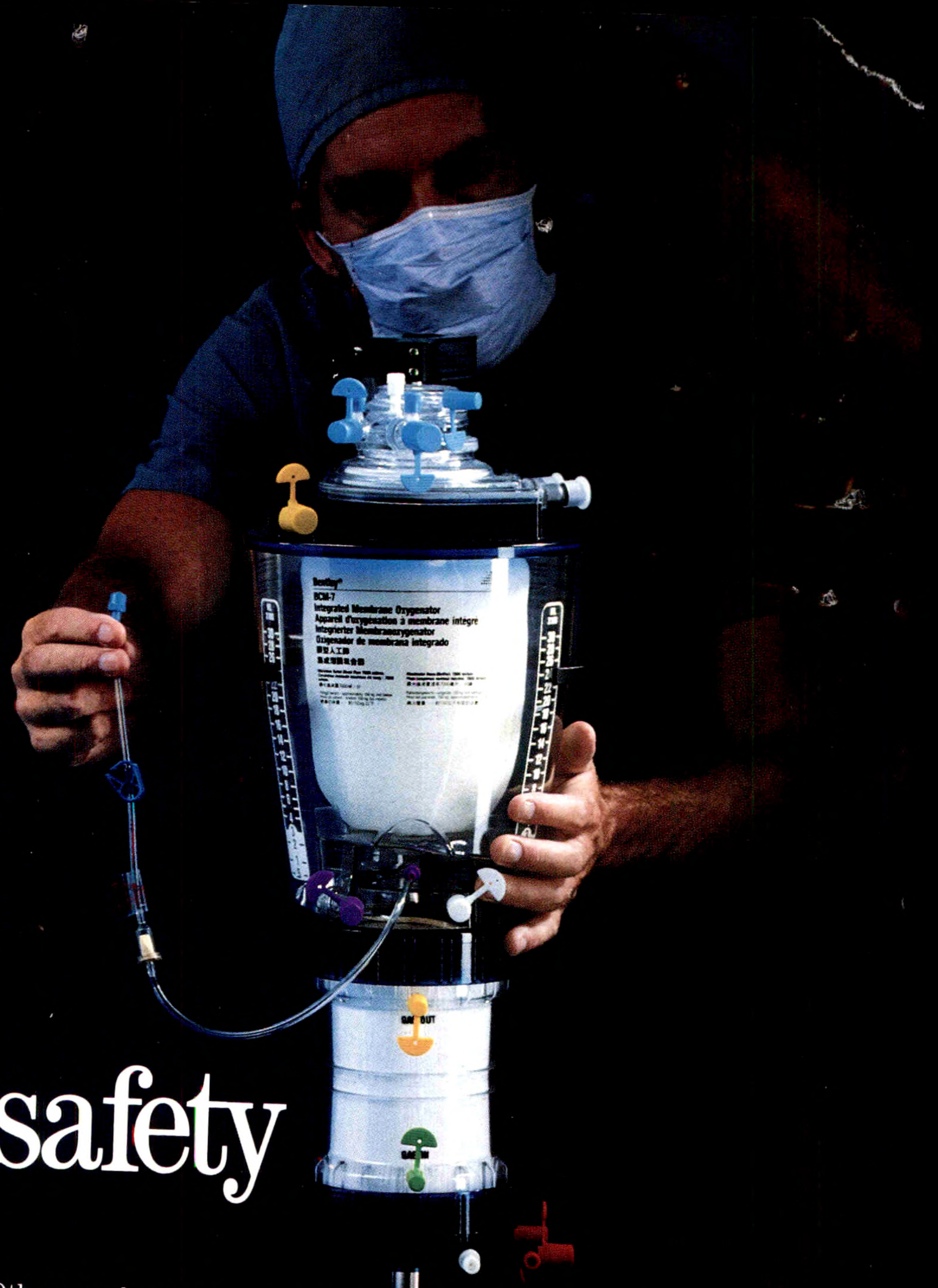

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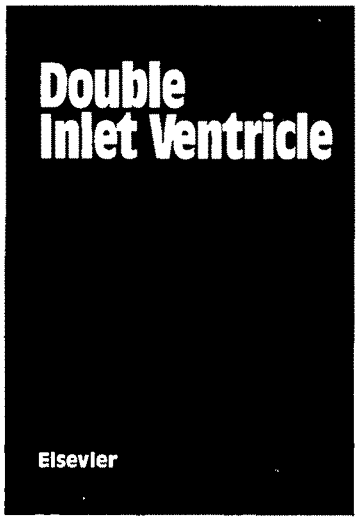

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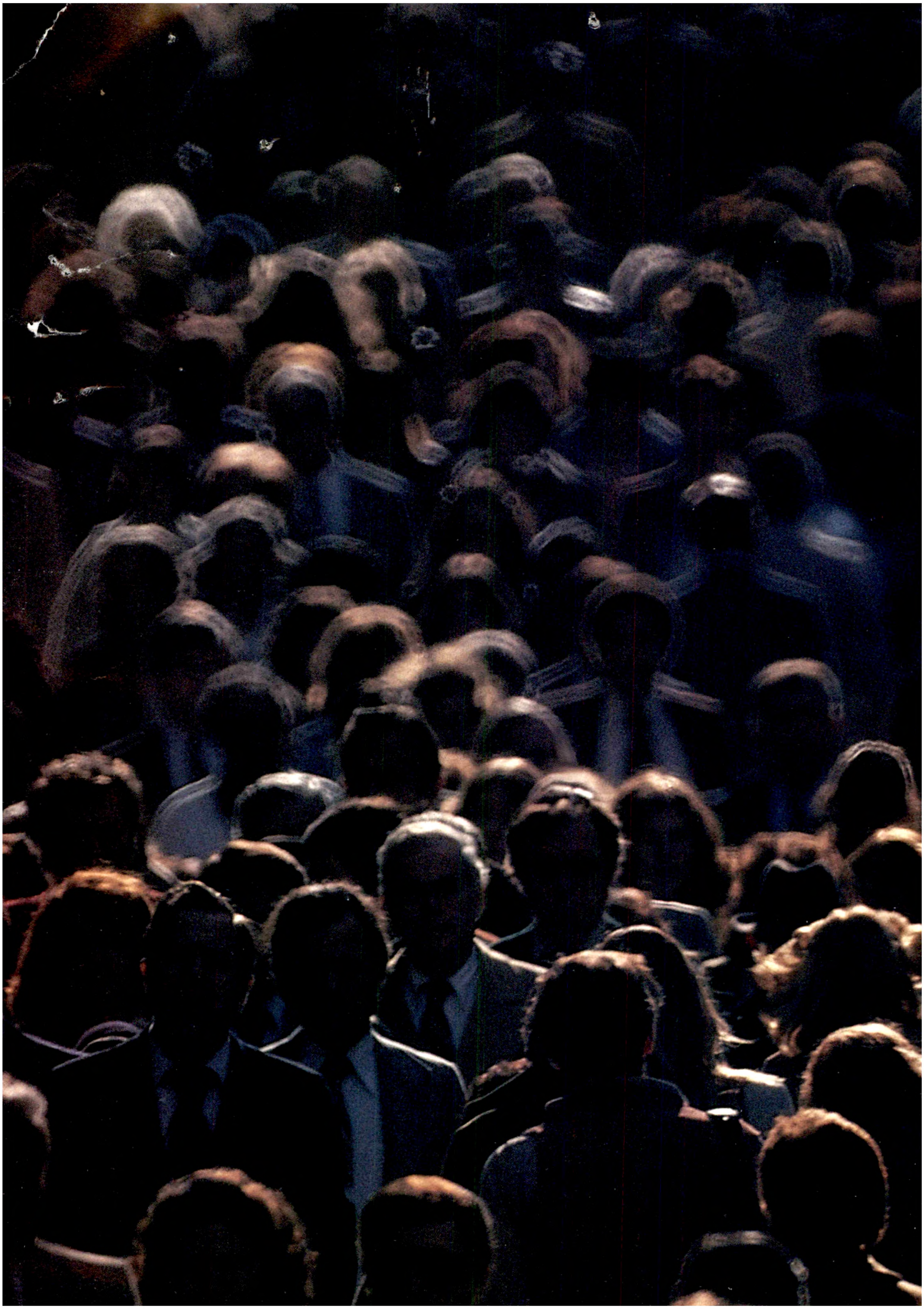

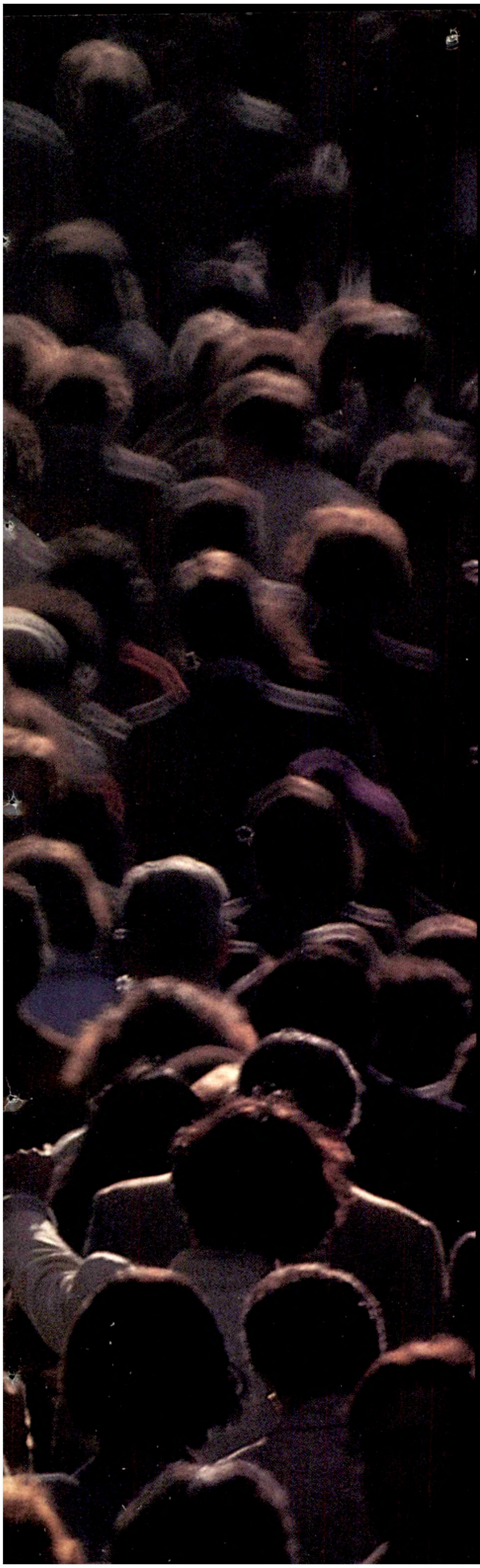

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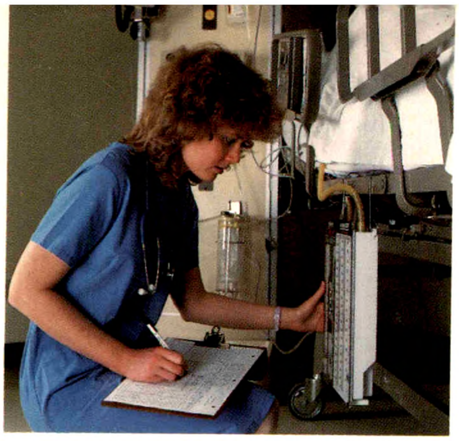

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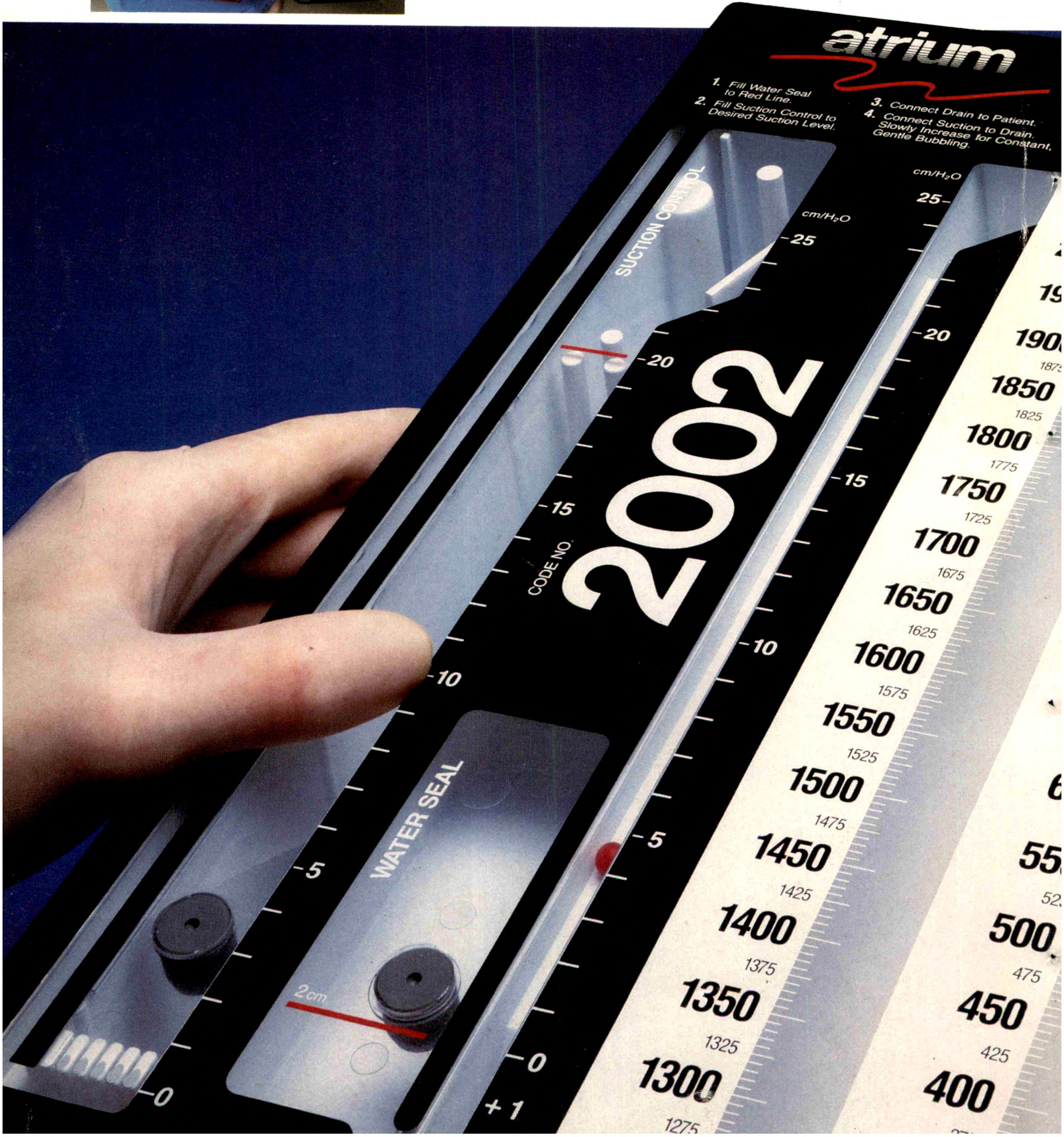
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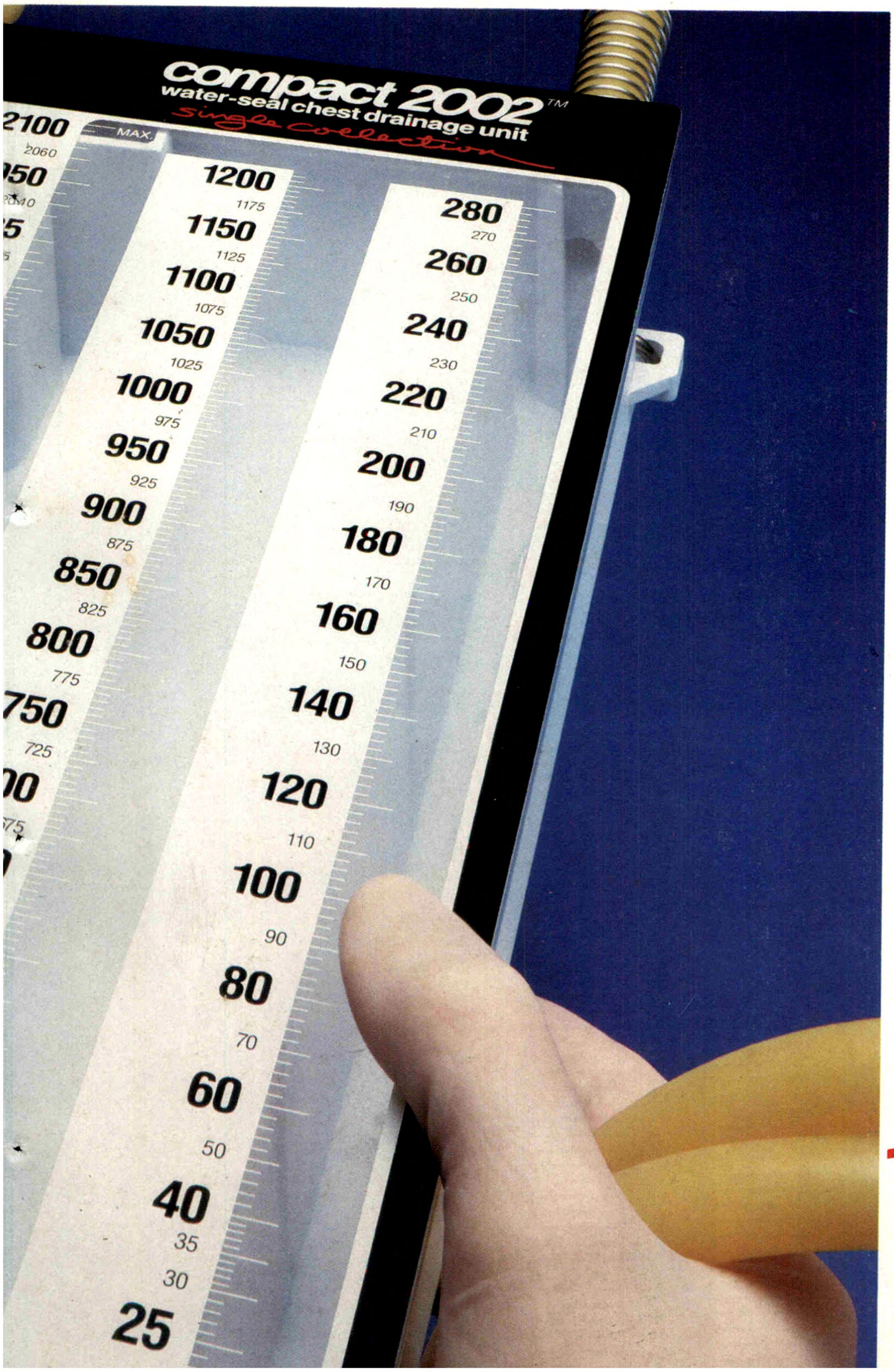

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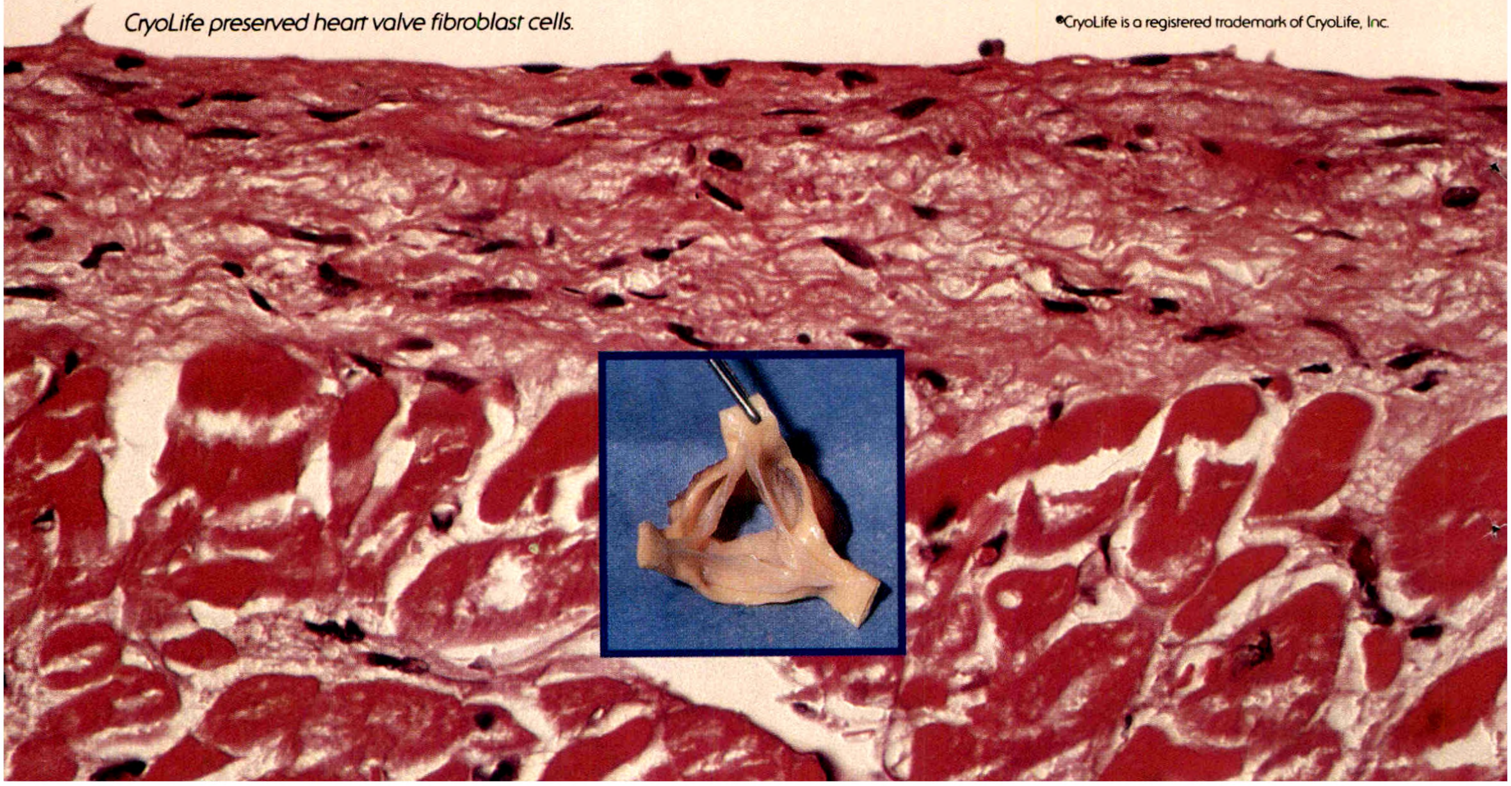

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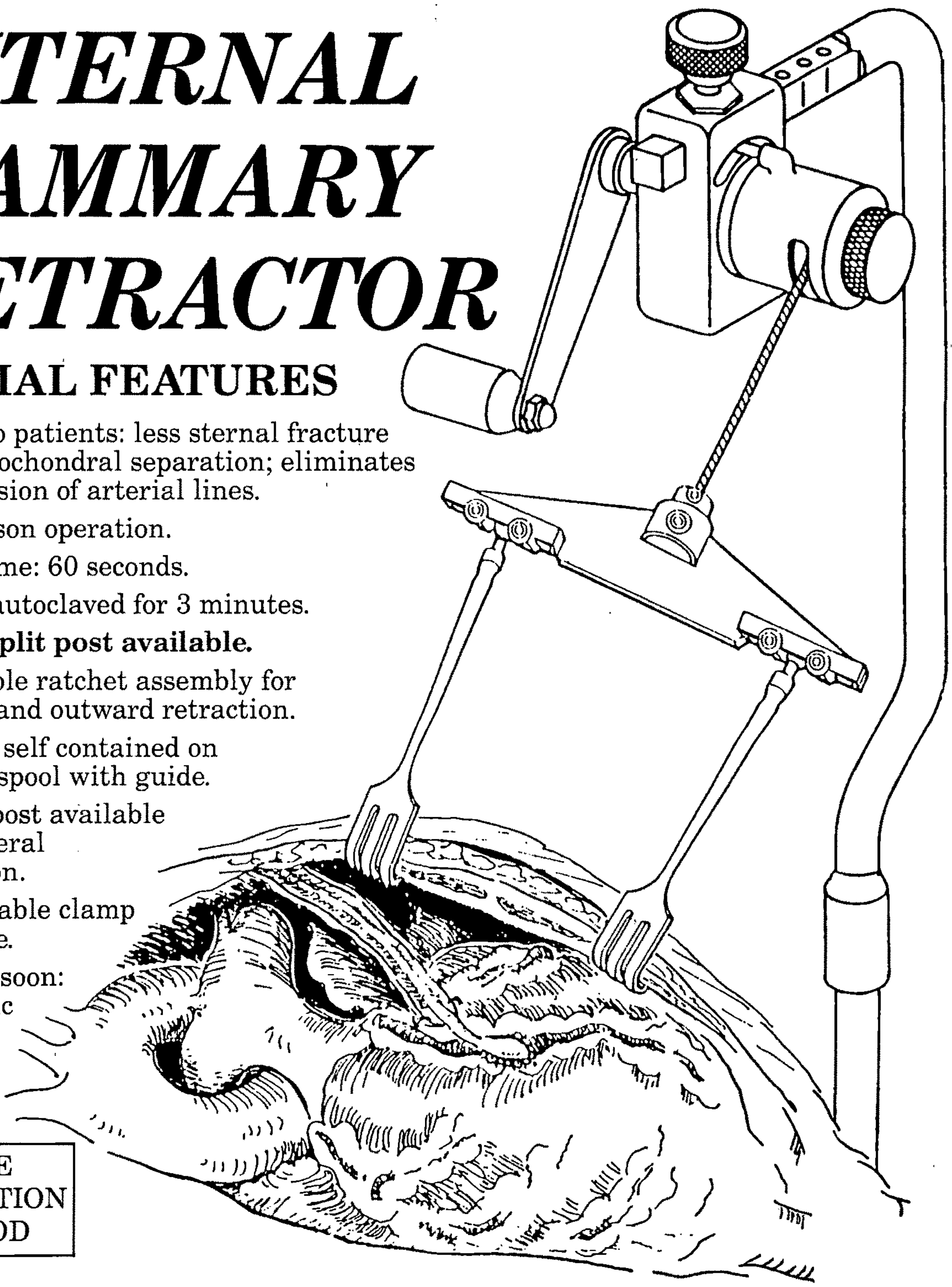

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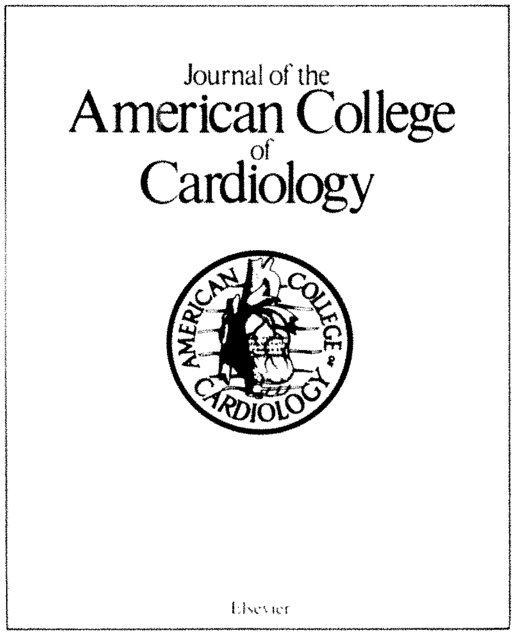

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The Pharmacological Treatment of Cardiovascular Diseases

Edited by

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Eugene A. DeFelice, M.D., Clinical Professor of Medicine, Division of Cardiovascular Diseases and Hypertension, UMDNJ-Rutgers Medical School, New Brunswick, New Jersey

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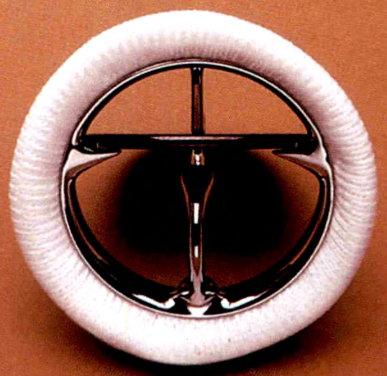


Medtronic Hancock® Valve: A strong record of reliability established by over 150,000 implants in over 17 years.

This clinical experience with the Hancock standard valve has demonstrated low thromboembolic incidence in the absence of anticoagulation. Further, the Hancock® Modified Orifice Valve provides excellent hemodynamics for the small aortic root.

Medtronic Duran Annuloplasty Ring: The flexible design gives physiologic results.

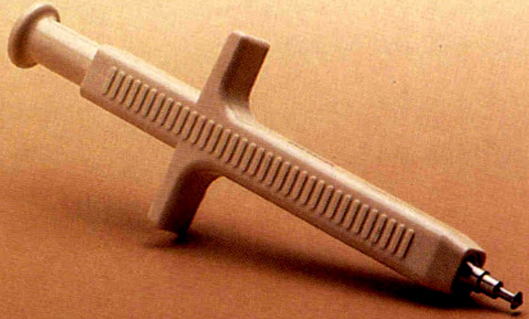
The unique flexible design of the Duran ring allows a larger mitral diastolic orifice resulting in better hemodynamics. The flexibility is also more compatible with normal ventricular movements. The ring minimizes the risk of dehiscence by reducing the tension on the sutures during systole. The ring is easy to size and suture through the Dacron* material.

---

*Dacron is a registered trademark of E.I. du Pont de Nemours & Company.

Medtronic Hancock® Aortic Punch: The leading disposable device for clean, circular openings.

Widely used in coronary artery bypass surgery, the Hancock Aortic Punch produces a clean, immediately patent opening in a patient's aorta that eliminates irregularities that can be associated with using a scalpel. The punch is designed for precision and ease of use.

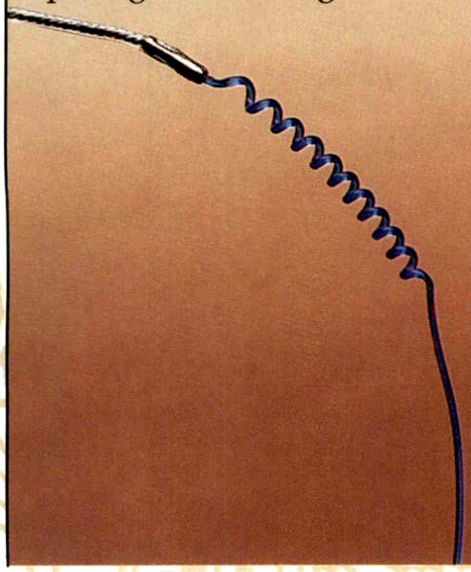


Medtronic Hall™ Aortic Valved Conduit Prosthesis: Improves safety, durability and procedural ease.

This conduit combines the benefits of the Medtronic Hall Valve – superior hemodynamics, proven durability, low thromboembolic risk – with that of a low porosity woven Dacron* graft, to improve patient safety.

Medtronic Model 6500 Temporary Heartwire: Improves postoperative pacing performance, enhances patient safety.

The unique fixation coil of this heartwire facilitates stable fixation and eliminates the need for sutures. It is flexible enough to be removed easily, minimizing trauma to cardiac tissue. The heartwire can be used in the atrium and the ventricle, and its discrete electrode provides superior pacing and sensing.



Our commitment to cardiovascular medicine began with pacing – where we are still the leaders. Today, our growth and research are extending to all aspects of cardiac reconstruction.

Making the heart
whole again.

Medtronic

For detailed information describing intended use, warnings, precautions, and contraindications, refer to the instructions provided with each device or contact your local Medtronic representative.

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MT VL-1107 R

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Intra-Aortic Balloon Pumping.

Because aggressive intervention saves lives.

Today hospitals of every size are using IABP to give their patients the greatest possible chance for survival.

More than 70% of all admissions related to ischemic heart disease present at hospitals which do not perform open-heart surgery. In the face of this statistic, hospitals large and small are intervening more aggressively, reducing the mortality rates dramatically. *And intra-aortic balloon pumping is significant in the achievement of these results.*

Datascope has been the innovative force in developing IABP as a life-saving therapy in hospitals of every size. Today, in fact, almost half of all the hospitals we serve do not have open-heart facilities. However, they are aggressively using IABP therapy to support many of their unstable cardiac patients.

A commitment to product innovation.
Since Datascope first introduced IABP in 1969, our resources have been dedicated to its steady development.

The System 90 console and 90T transport balloon pumps

represent fifth generation technology. The simple, automatic operation of these systems has resulted in more Datascope units being put into service than all other pumps combined.

Steady improvements in safety and ease of catheter insertion (from our introduction of the first percutaneous balloon catheter to our newest prefolded 9.5 French dual lumen catheter) have resulted in more aggressive use of IABP therapy at the earliest indication.

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Datascope's Clinical Education Services Department offers a level of support second to none in IABP, and rare even within the field of cardiac care.

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With our staff of over 50 technical service representatives dedicated exclusively to your Datascope products, you can depend on us for routine and emergency maintenance 24 hours a day, seven days a week. To make certain you are never without the use of your equipment, loaner units are available. And because there are occasional unplanned demands for IABP, we can help you meet unexpected requirements through our equipment rental program.

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For information and assistance, call (201) 265-8800. Or write: Datascope, P.O. Box 5, Paramus, NJ 07653-0005.

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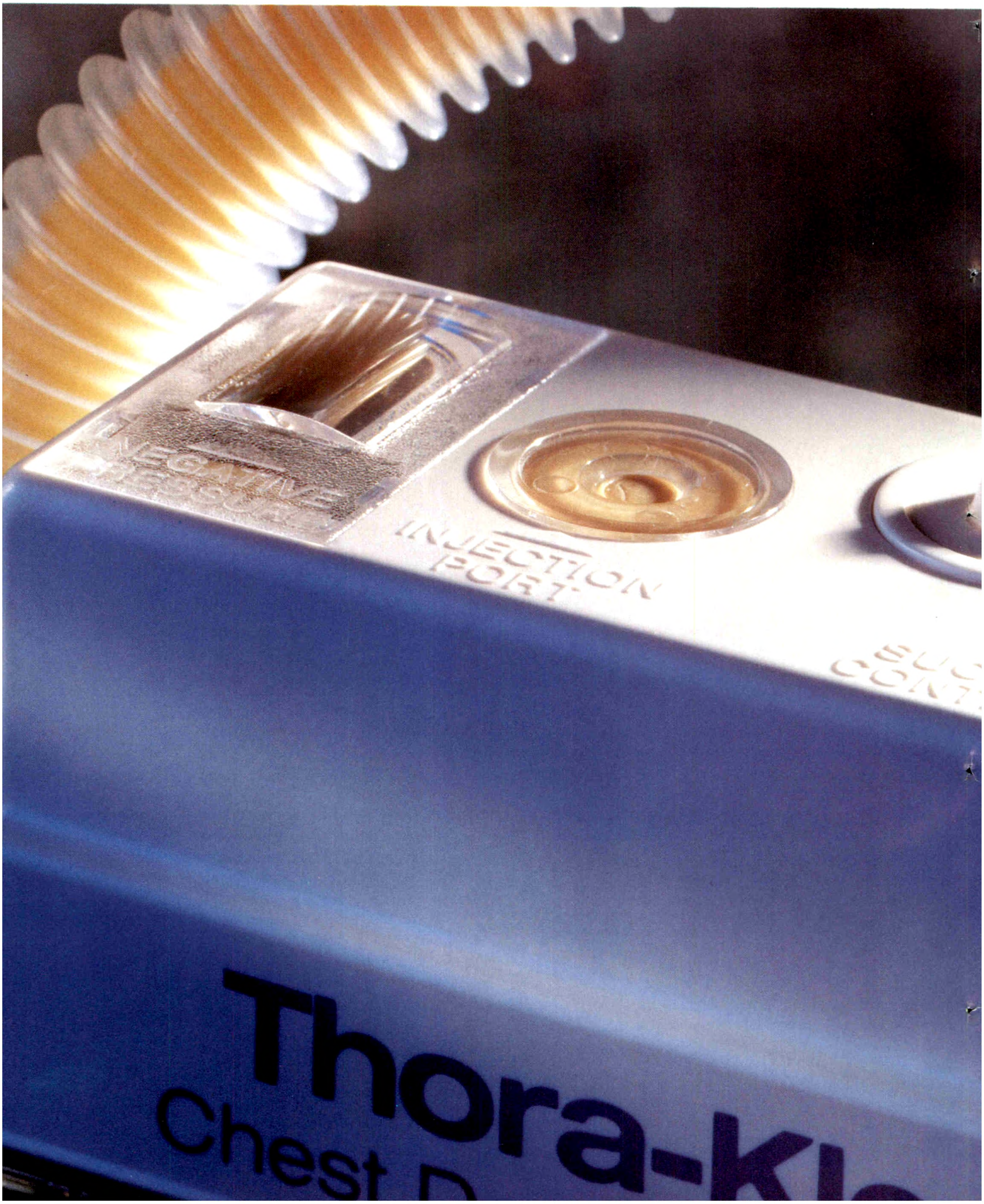

plete family of chest drainage systems and the Thora-Klex Autotransfusion Kit.

Use the Thora-Klex 2500ml System for standard thoracic and cardiovascular procedures; the Thora-Klex 4000ml Dual Collection System for emergency, trauma, and multiple chest tube procedures; and the Thora-Klex 350ml procedures. The Thora-Klex Autotransfusion Kit may be used with the 2500ml and 4000ml units for safe, simple blood collection and reinfusion. A line of quality chest catheters is also available for the Thora-Klex Systems.

For more information and a product demonstration, call 1-800-556-6275.

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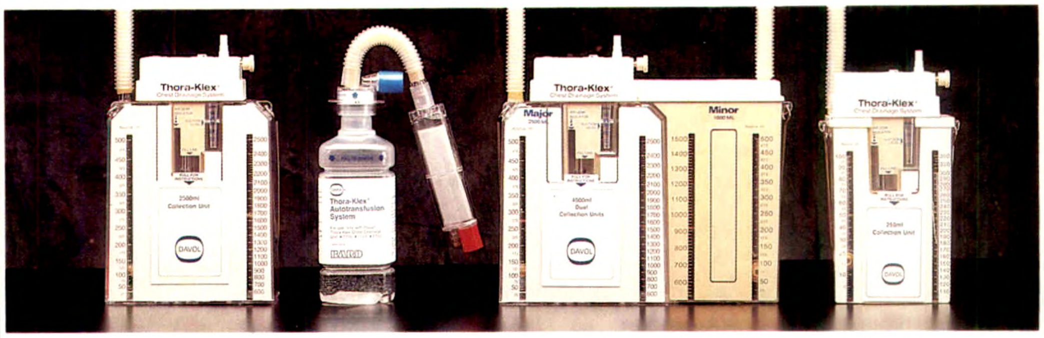
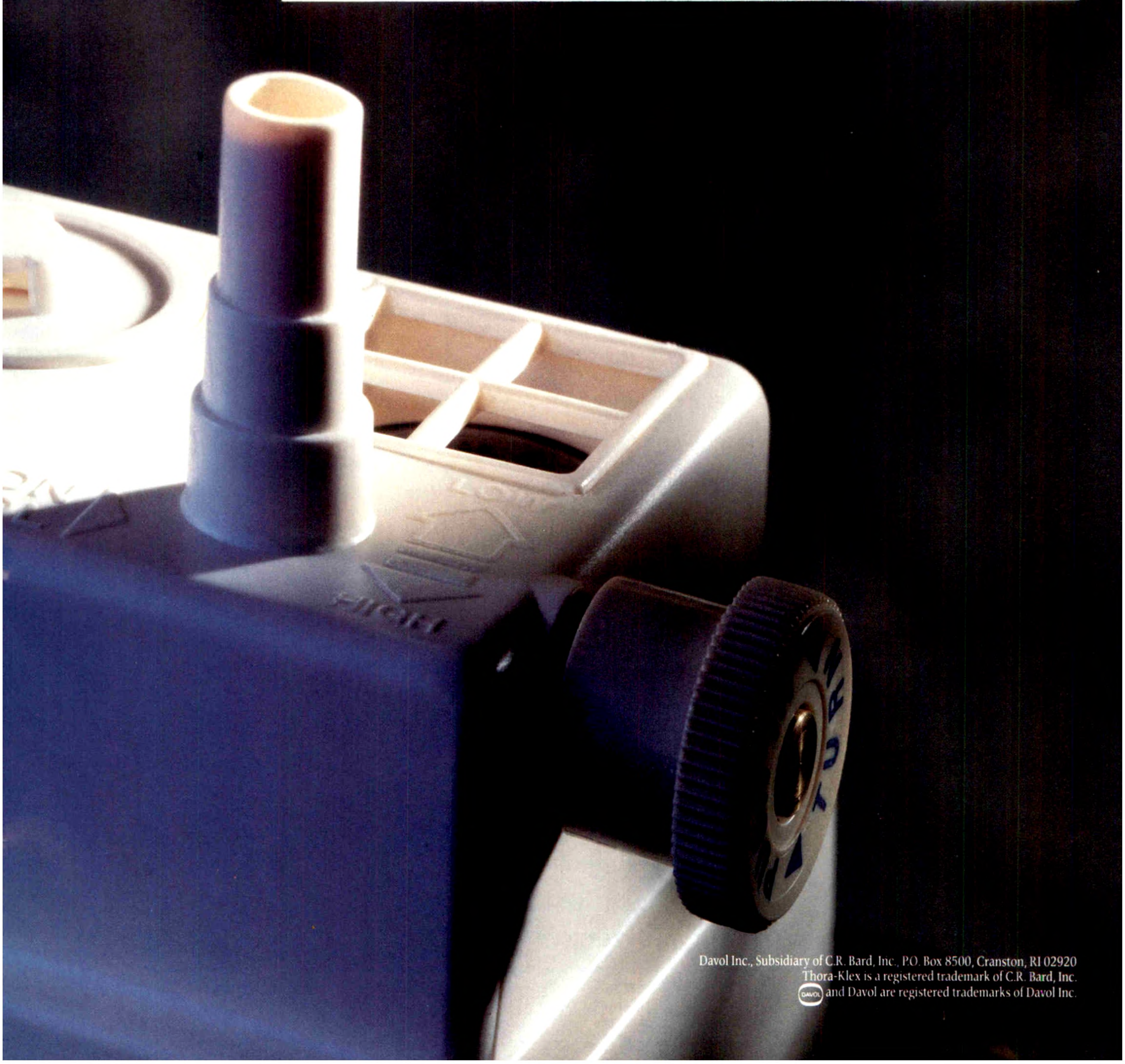


Thora-Klex 2500ml System

Thora-Klex Autotransfusion Kit

Thora-Klex 4000ml System

Thora-Klex 350ml System



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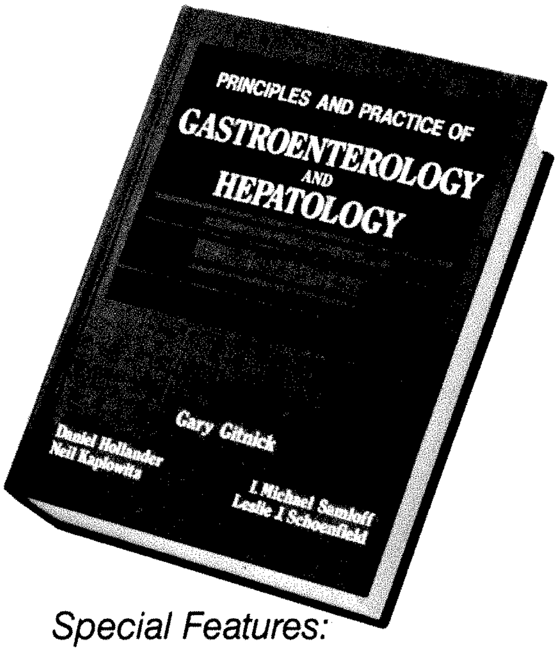

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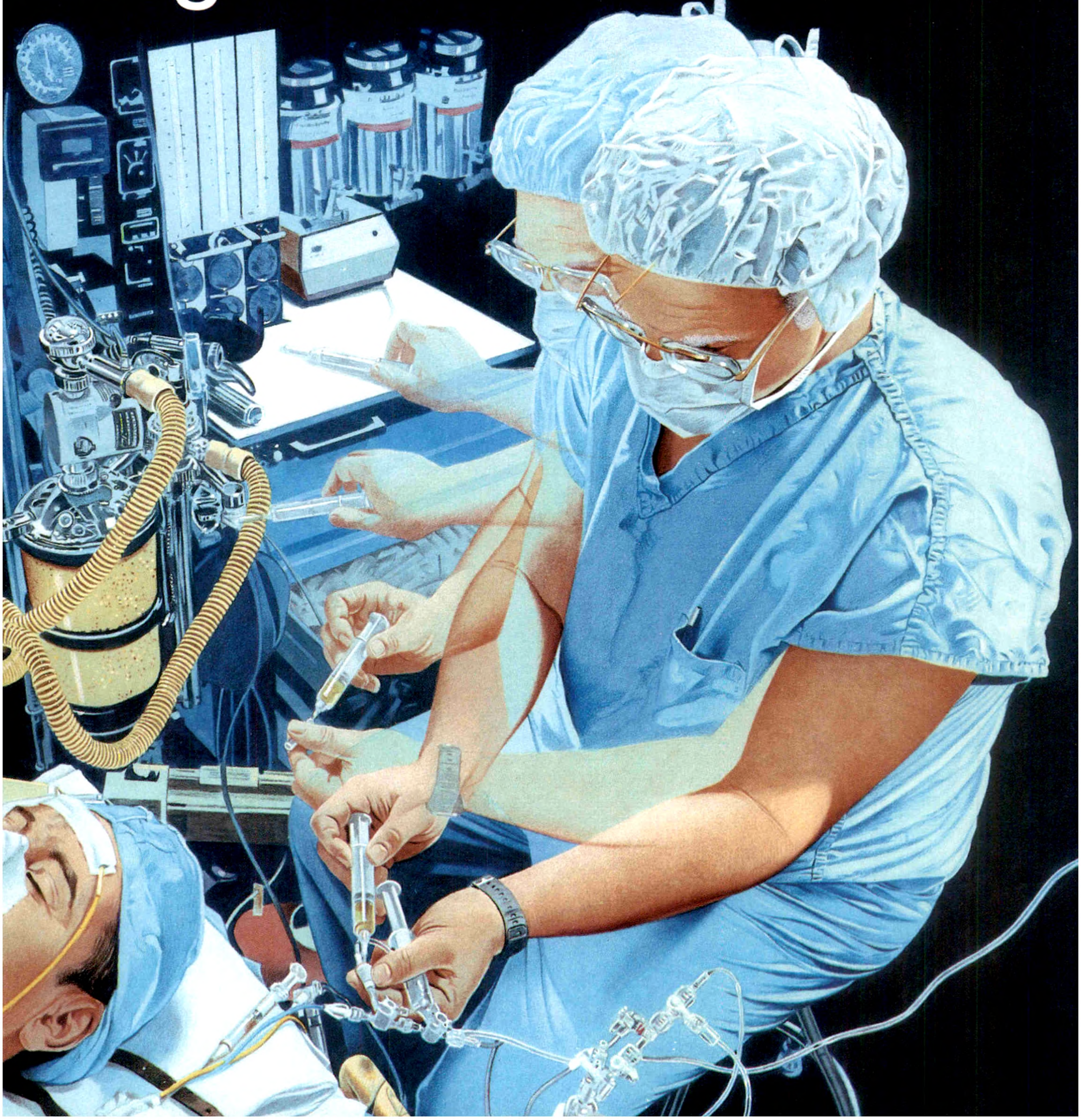

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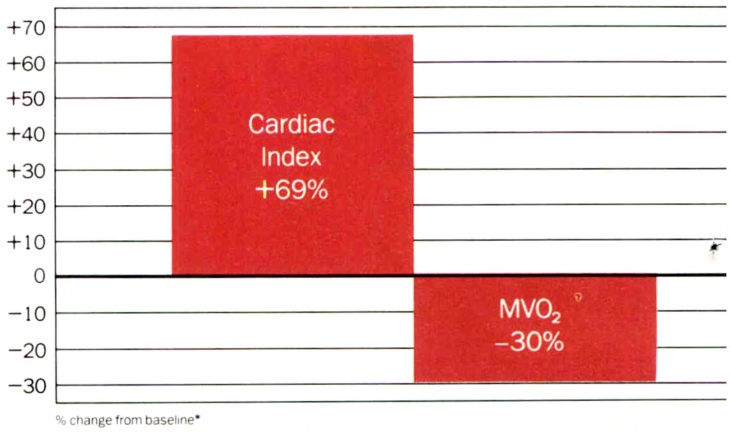
INOCOR I.V. (amrinone) provides improved hemodynamics without raising MVO_2 and worsening myocardial ischemia[1]

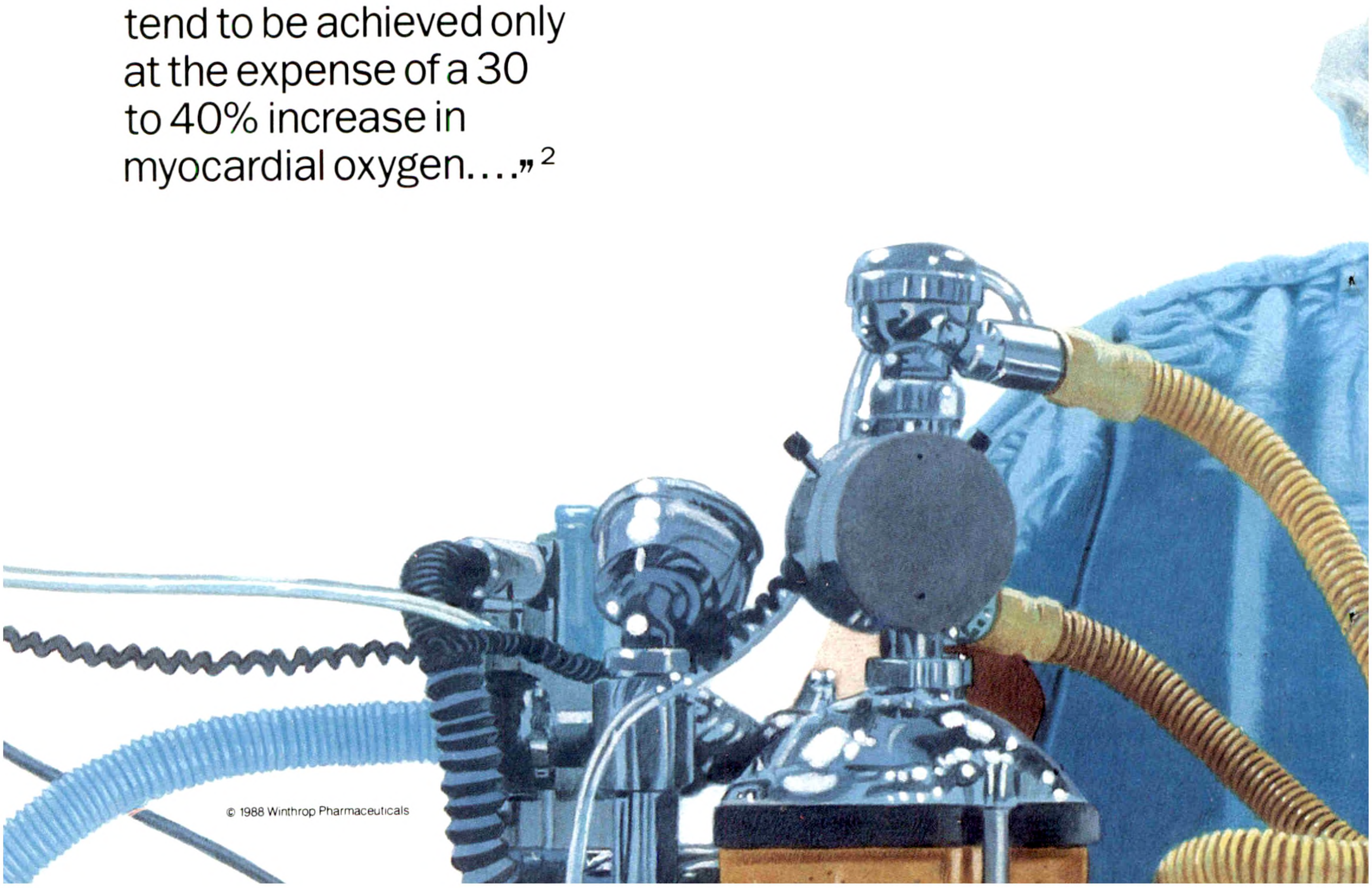


*n=8. Adapted from Benotti et al.[1] Amrinone was infused in patients with severe congestive heart failure due to coronary artery disease at 2.5 mg/kg over 1 hour.

1. Benotti JR, Grossman W, Braunwald E, et al: Effects of amrinone on myocardial energy metabolism and hemodynamics in patients with severe congestive heart failure due to coronary artery disease. *Circulation* 1980;62:28–34.

2. Baim DS: Effects of amrinone on myocardial energetics in severe congestive heart failure. *Am J Cardiol* 1985;56:16B–18B.

"...hemodynamic improvements with catecholamine agents such as dobutamine tend to be achieved only at the expense of a 30 to 40% increase in myocardial oxygen...."[2]



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- Unique mechanism of action—PDE III inhibition
- Significantly improves pulmonary hemodynamics
- Efficacy maintained even in patients on beta blockers
- Does not increase the risk of arrhythmias (see Precautions)

Dual-acting, energy-efficient

Inocor® I.V.

(AMRINONE)

Raises output without raising MVO_2

Please see following page for important product information concerning contraindications, warnings, adverse reactions, patient selection, and prescribing and precautionary recommendations.

INOCOR I.V.: Potent inotropic action in low output syndrome without increasing MVO_2 or aggravating myocardial ischemia

- A unique mode of action—selective PDE III inhibition
- No effect on platelet function
- No significant increase in risk of arrhythmias (see Precautions)
- Safe and effective when used concomitantly with intravenous or inhaled anesthetics
- Unlike catecholamines, does not act on the beta receptors—may be used effectively in patients on beta blockers

Brief Summary

Please consult full product information before prescribing. A summary follows. INOCOR lactate injection, brand of amrinone lactate, represents a new class of cardiac inotropic agents with vasodilator activity, distinct from digitalis glycosides or catecholamines.

INDICATIONS AND USAGE INOCOR lactate injection is indicated for the short-term management of congestive heart failure. Because of limited experience and potential for serious adverse effects (see ADVERSE REACTIONS), INOCOR should be used only in patients who can be closely monitored and who have not responded adequately to digitalis, diuretics, and/or vasodilators. Although most patients have been studied hemodynamically for periods only up to 24 hours, some patients were studied for longer periods and demonstrated consistent hemodynamic and clinical effects. The duration of therapy should depend on patient responsiveness.

CONTRAINDICATIONS INOCOR lactate injection is contraindicated in patients who are hypersensitive to it. It is also contraindicated in those patients known to be hypersensitive to bisulfites.

PRECAUTIONS *General:* INOCOR lactate injection should not be used in patients with severe aortic or pulmonic valvular disease in lieu of surgical relief of the obstruction. Like other inotropic agents, it may aggravate outflow tract obstruction in hypertrophic subaortic stenosis.

During intravenous therapy with INOCOR lactate injection, blood pressure and heart rate should be monitored and the rate of infusion slowed or stopped in patients showing excessive decreases in blood pressure.

Patients who have received vigorous diuretic therapy may have insufficient cardiac filling pressure to respond adequately to INOCOR lactate injection, in which case cautious liberalization of fluid and electrolyte intake may be indicated.

Supraventricular and ventricular arrhythmias have been observed in the very high-risk population treated. While amrinone per se has not been shown to be arrhythmogenic, the potential for arrhythmia, present in congestive heart failure itself, may be increased by any drug or combination of drugs.

Thrombocytopenia and hepatotoxicity have been noted (see ADVERSE REACTIONS).

INOCOR is not recommended for use in acute myocardial infarction.

LABORATORY TESTS *Fluid and electrolytes:* Fluid and electrolyte changes and renal function should be carefully monitored during amrinone lactate therapy. Improvement in cardiac output with resultant diuresis may necessitate a reduction in the dose of diuretic. Potassium loss due to excessive diuresis may predispose digitalized patients to arrhythmias. Therefore, hypokalemia should be corrected by potassium supplementation in advance of or during amrinone use.

DRUG INTERACTIONS In a relatively limited experience, no untoward clinical manifestations have been observed in patients in whom INOCOR lactate injection was used concurrently with the following drugs: digitalis glycosides; lidocaine, quinidine; metoprolol, propranolol; hydralazine, prazosin; isosorbide dinitrate, nitroglycerine; chlorthalidone, ethacrynic acid, furosemide, hydrochlorothiazide, spironolactone; captopril; heparin, warfarin; potassium supplements; insulin; diazepam.

One case of excessive hypotension was reported when amrinone was used concurrently with disopyramide.

Until additional experience is available, concurrent administration with Norpace® (disopyramide) should be undertaken with caution.

CHEMICAL INTERACTIONS A chemical interaction occurs slowly over a 24-hour period when the intravenous solution of INOCOR lactate injection is mixed directly with dextrose (glucose)-containing solutions. **THEREFORE, INOCOR LACTATE INJECTION SHOULD NOT BE DILUTED WITH SOLUTIONS THAT CONTAIN DEXTROSE (GLUCOSE) PRIOR TO INJECTION.**

A chemical interaction occurs immediately, which is evidenced by the formation of a precipitate when furosemide is injected into an intravenous line of an infusion of amrinone. Therefore, furosemide should not be administered in intravenous lines containing amrinone.

USE IN PREGNANCY *Pregnancy category C:* There are no adequate and well-controlled studies in pregnant women. Amrinone should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

USE IN NURSING MOTHERS Caution should be exercised when amrinone is administered to nursing women, since it is not known whether it is excreted in human milk.

USE IN CHILDREN Safety and effectiveness in children have not been established.

ADVERSE REACTIONS *Thrombocytopenia:* Intravenous INOCOR lactate injection resulted in platelet count reductions to below 100,000/mm^3 or normal limits in 2.4% of patients.

Gastrointestinal effects: Gastrointestinal adverse reactions reported with INOCOR lactate injection during clinical use included nausea (1.7%), vomiting (0.9%), abdominal pain (0.4%), and anorexia (0.4%).

Cardiovascular effects: Cardiovascular adverse reactions reported with INOCOR lactate injection include arrhythmia (3%) and hypotension (1.3%).

Hepatic toxicity: In dogs, at IV doses between 9 mg/kg/day and 32 mg/kg/day, amrinone showed dose-related hepatotoxicity manifested either as enzyme elevation or hepatic cell necrosis or both. Hepatotoxicity has been observed in man following long-term oral dosing and has been observed, in a limited experience (0.2%), following IV administration of amrinone.

Hypersensitivity: There have been reports of several apparent hypersensitivity reactions in patients treated with oral amrinone for about two weeks. Signs and symptoms were variable but included pericarditis, pleuritis, and ascites (one case); myositis with interstitial shadowing on chest x-ray and elevated sedimentation rate (one case); and vasculitis with nodular pulmonary densities, hypoxemia, and jaundice (one case). The first patient died, not necessarily of the possible reaction, while the last two resolved with discontinuation of therapy. None of the cases were rechallenged, so attribution to amrinone is not certain, but possible hypersensitivity reactions should be considered in any patient maintained for a prolonged period on amrinone.

General: Additional adverse reactions observed in intravenous amrinone clinical studies include fever (0.9%), chest pain (0.2%), and burning at the site of injection (0.2%).

MANAGEMENT OF ADVERSE REACTIONS *Platelet count reductions:* Asymptomatic platelet count reduction (to less than 150,000/mm^3) may be reversed within one week of a decrease in drug dosage. Further, with no change in drug dosage, the count may stabilize at lower than predrug levels without any clinical sequelae. Predrug platelet counts and frequent platelet counts during therapy are recommended to assist in decisions regarding dosage modifications.

Should a platelet count less than 150,000/mm^3 occur, the following actions may be considered:

- Maintain total daily dose unchanged, since in some cases counts have either stabilized or returned to pretreatment levels.
- Decrease total daily dose.
- Discontinue amrinone if, in the clinical judgment of the physician, risk exceeds the potential benefit.

Gastrointestinal side effects: While gastrointestinal side effects were seen infrequently with IV therapy, should severe or debilitating ones occur, the physician may wish to reduce dosage or discontinue the drug based on the usual benefit-to-risk considerations.

Hepatic toxicity: In clinical experience to date with IV administration, hepatotoxicity has rarely been observed. If acute marked alterations in liver enzymes occur together with clinical symptoms, suggesting an idiosyncratic hypersensitivity reaction, amrinone therapy should be promptly discontinued.

If less than marked enzyme alterations occur without clinical symptoms, these nonspecific changes should be evaluated on an individual basis. The clinician may wish to continue amrinone, reduce dosage, or discontinue the drug based on the usual benefit-to-risk considerations.

OVERDOSAGE Doses of INOCOR lactate injection may produce hypotension because of its vasodilator effect. If this occurs, amrinone administration should be reduced or discontinued. No specific antidote is known, but general measures for circulatory support should be taken.

HOW SUPPLIED Ampuls of 20 mL sterile, clear yellow solution containing INOCOR 5 mg/mL, box of 5 (NDC 0024-0888-20). Each 1 mL contains INOCOR lactate equivalent to 5 mg base and 0.25 mg sodium metabisulfite in Water for Injection. The pH of INOCOR lactate injection is adjusted to a range of 3.2 to 4.0 with lactic acid or sodium hydroxide.

Protect INOCOR lactate ampuls from light. Ampul packaging is light resistant for protection during storage.

Store at room temperature.

NOTE: Parenteral drug products should be inspected visually and should not be used if particulate matter or discoloration is observed.

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Dual-acting, energy-efficient

Inocor® I.V.

(AMRINONE)

Raises output without raising MVO_2

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For further product information, call 800-526-2459.
Please see following page for brief summary of prescribing information.
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THROMBOGEN*
(THROMBIN, USP) (Bovine Origin)

Before prescribing, please see full prescribing information. A Brief Summary follows:
THROMBOGEN* must not be injected! Apply on the surface of bleeding tissue as a solution or powder.

INDICATIONS AND USAGE: THROMBOGEN* (Thrombin, USP) is indicated as an aid in hemostasis wherever oozing blood from capillaries and small venules is accessible.
In various types of surgery solutions of THROMBOGEN* may be used in conjunction with Absorbable Gelatin Sponge, USP for hemostasis.

CONTRAINDICATIONS: THROMBOGEN* is contraindicated in persons known to be sensitive to any of its components and/or to material of bovine origin.

WARNING: Because of its action in the clotting mechanism, THROMBOGEN* must not be injected or otherwise allowed to enter large blood vessels. Extensive intravascular clotting and even death may result. THROMBOGEN* is an antigenic substance and has caused sensitivity and allergic reactions when injected into animals.

PRECAUTIONS: General: Consult the absorbable gelatin sponge product labeling for complete information for use prior to utilizing the thrombin-saturated-sponge procedure.
Pregnancy-Teratogenic effects: Pregnancy Category C. Animal reproduction studies have not been conducted with Thrombin, Topical (Bovine). It is also not known whether Thrombin, Topical (Bovine) can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Thrombin, Topical (Bovine) should be given to a pregnant woman only if clearly indicated.
Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS: An allergic type reaction following the use of THROMBOGEN* for treatment of epistaxis has been reported. Febrile reactions have also been observed following the use of THROMBOGEN* in certain surgical procedures but no cause-effect relationship has been established.

DOSAGE AND ADMINISTRATION: General: Solutions of THROMBOGEN* may be prepared in sterile distilled water or isotonic saline. The intended use determines the strength of the solution to prepare. For general use in plastic surgery, dental extractions, skin grafting, neurosurgery, etc., solutions containing approximately 100 units per ml. are frequently used. For this, 10 ml. of diluent added to the 1,000 unit package is suitable. Where bleeding is profuse, as from cut surfaces of liver and spleen, concentrations as high as 1,000 to 2,000 units per ml. may be required. For this the 5,000 unit vial dissolved in 5 ml. or 2.5 ml., respectively, of the diluent supplied in the package is convenient. Intermediate strengths to suit the needs of the case may be prepared by selecting the proper strength package and dissolving the contents in an appropriate volume of diluent. In many situations, it may be advantageous to use THROMBOGEN* (Thrombin, USP) in dry form on oozing surfaces.
Caution: Solutions should be used immediately upon reconstitution. However, the solution may be refrigerated at 2–8°C for up to three hours. The following techniques are suggested for the topical application of THROMBOGEN:*

1. The recipient surface should be sponged (not wiped) free of blood before THROMBOGEN* is applied.
2. A spray may be used or the surface may be flooded using a sterile syringe and small gauge needle. The most effective hemostasis results when the THROMBOGEN* mixes freely with the blood as soon as it reaches the surface.
3. In instances where THROMBOGEN* in dry form is needed, the vial is opened by removing the metal ring by flipping up the plastic cap and tearing counterclockwise. The rubber-diaphragm cap may be easily removed and the dried THROMBOGEN* is then broken up into a powder by means of a sterile glass rod or other suitable sterile instrument.
4. Sponging of treated surfaces should be avoided in order that the clot remain securely in place.
   THROMBOGEN* may be used in conjunction with Absorbable Gelatin Sponge, USP as follows:
   1. Prepare THROMBOGEN* solution of the desired strength.
   2. Immerse sponge strips of the desired size in the THROMBOGEN* solution. Knead the sponge strips vigorously with moistened gloved fingers to remove trapped air, thereby facilitating saturation of the sponge.
   3. Apply saturated sponge to bleeding area. Hold in place for 10 to 15 seconds with a pledget of cotton or a small gauze sponge.

THROMBOGEN* Spray Kit: The THROMBOGEN* Spray Kit contains one sterile vial of THROMBOGEN,* one sterile vial of isotonic saline diluent, one sterile disposable syringe and one sterile syringe spray tip. The kit may be used as follows:

1. Remove the Tyvek† blister lid from the outermost tray by pulling up at the indicated corner. The sterile inner tray can then be lifted out or introduced into the sterile field.
2. Remove the Tyvek† blister lid from the inner tray to expose the sterile contents.
3. Using the sterile syringe equipped with the needle, draw the desired amount of saline diluent from the vial into the syringe.
4. Inject the saline diluent into the THROMBOGEN* vial from the syringe to reconstitute the THROMBOGEN* powder.
5. When the THROMBOGEN* is completely dissolved, draw the THROMBOGEN* solution into the syringe.
6. Remove and discard the needle; affix spray tip by pushing down and turning clockwise until the spray tip locks in place.
7. Depress the syringe plunger in a normal fashion to dispense the THROMBOGEN* solution through the tip in a fine spray.
8. Alternatively, to facilitate using the THROMBOGEN* with an Absorbable Gelatin Sponge, USP, the THROMBOGEN* solution may be dispensed directly from the syringe into a sterile container vs. attaching the spray tip. When THROMBOGEN* is needed in the dry form, the vial is opened and the dried THROMBOGEN* pellet should be broken up into a powder with a sterile glass rod or other suitable instrument.

Caution: Federal law prohibits dispensing without a prescription.
THROMBOGEN* is manufactured by GenTrac, Inc.
Middleton, WI 53562
*Trademark of Johnson & Johnson Patient Care, Inc.
†Trademark of DuPont.
Store at normal controlled room temperature, except 1,000 unit vial of THROMBOGEN,* which must be stored between 2°–8°C (36°–46°F).
For further product information, call 1-800-526-2459.
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The Pharmacological Treatment of Cardiovascular Diseases

Edited by
John B. Kostis, M.D., Professor of Medicine and Chief, Division of Cardiovascular Diseases and Hypertension, UMDNJ-Rutgers Medical School, New Brunswick, New Jersey
Eugene A. DeFelice, M.D., Clinical Professor of Medicine, Division of Cardiovascular Diseases and Hypertension, UMDNJ-Rutgers Medical School, New Brunswick, New Jersey

This brand new volume presents a complete survey of the pharmacological treatment of cardiovascular diseases. Comprehensive descriptions of the manifestations of a wide range of cardiovascular diseases and their pathophysiology are detailed in this 408 page, 22 chapter text. Highlighted are all aspects of those disorders most commonly encountered in clinical practice and the appropriate pharmacologic agents needed for effective treatment.

The text is divided into sections that provide in-depth coverage of the following topics:

- Hypertension
- Heart Failure
- Angina Pectoris
- Myocardial Infarction
- Arrhythmias

The Pharmacological Treatment of Cardiovascular Diseases also contains these useful features:

- Summary tables showing drug comparisons, their efficacy, and adverse reactions
- Reference lists at the end of each chapter that provide information for further study

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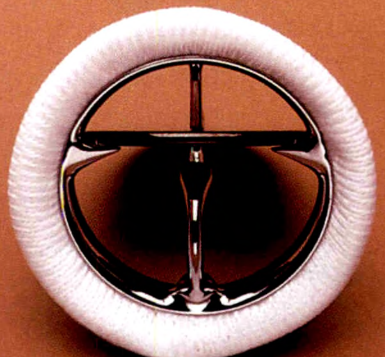

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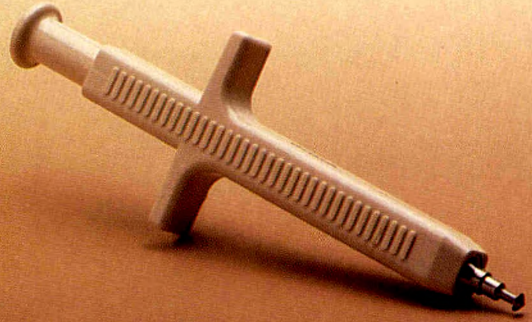

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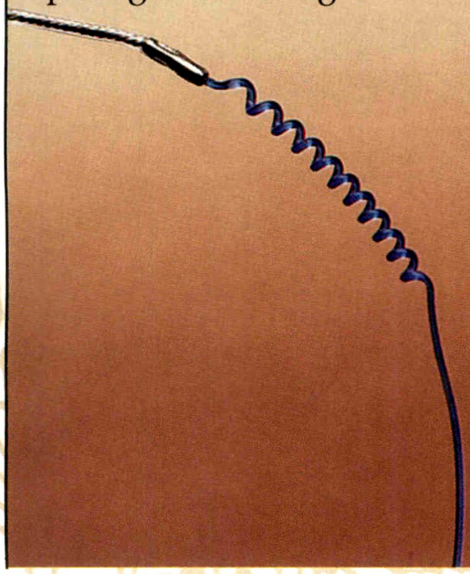

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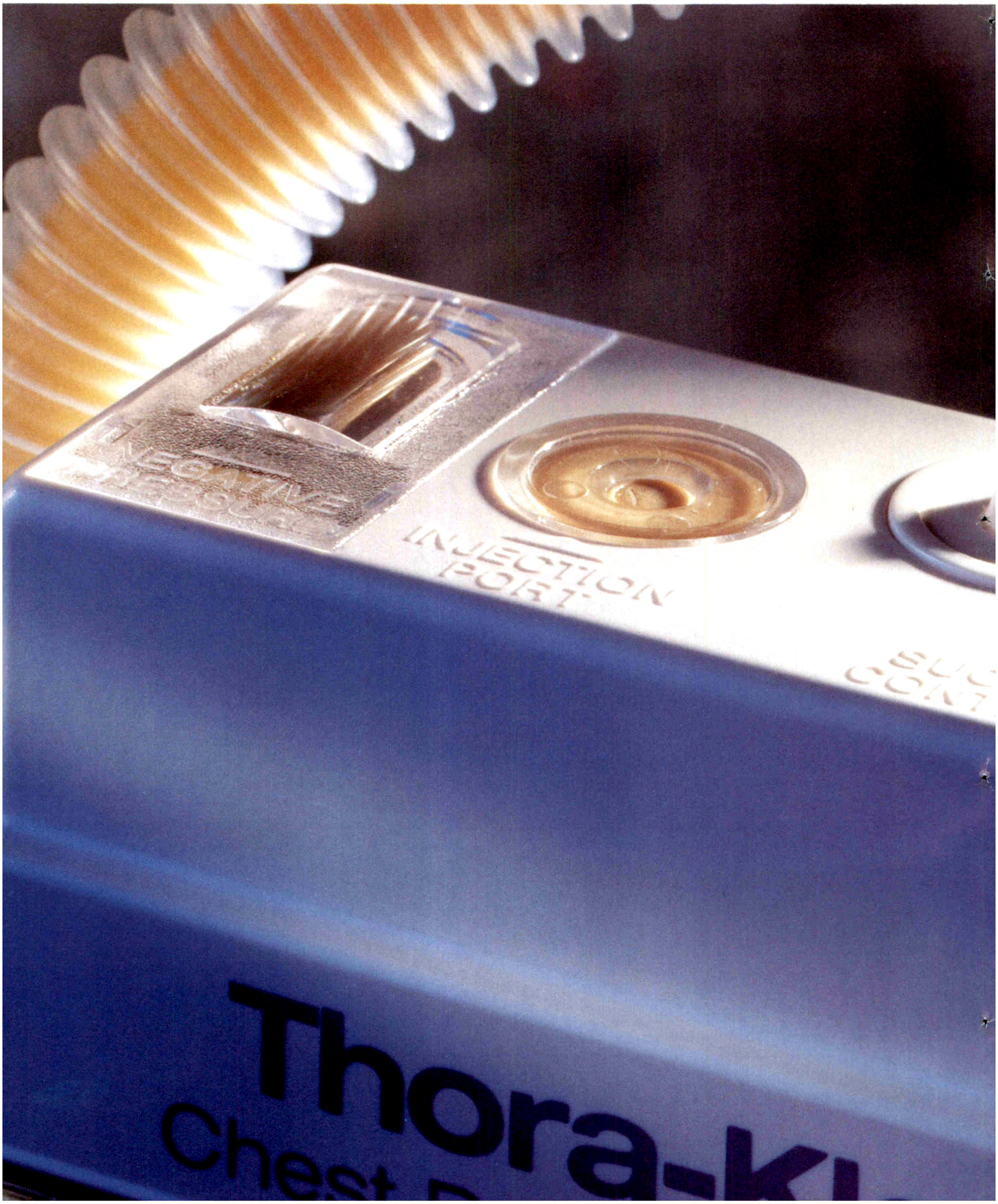

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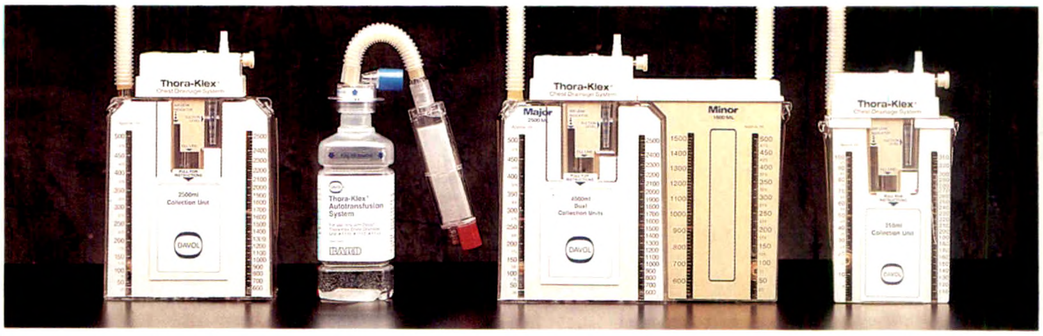

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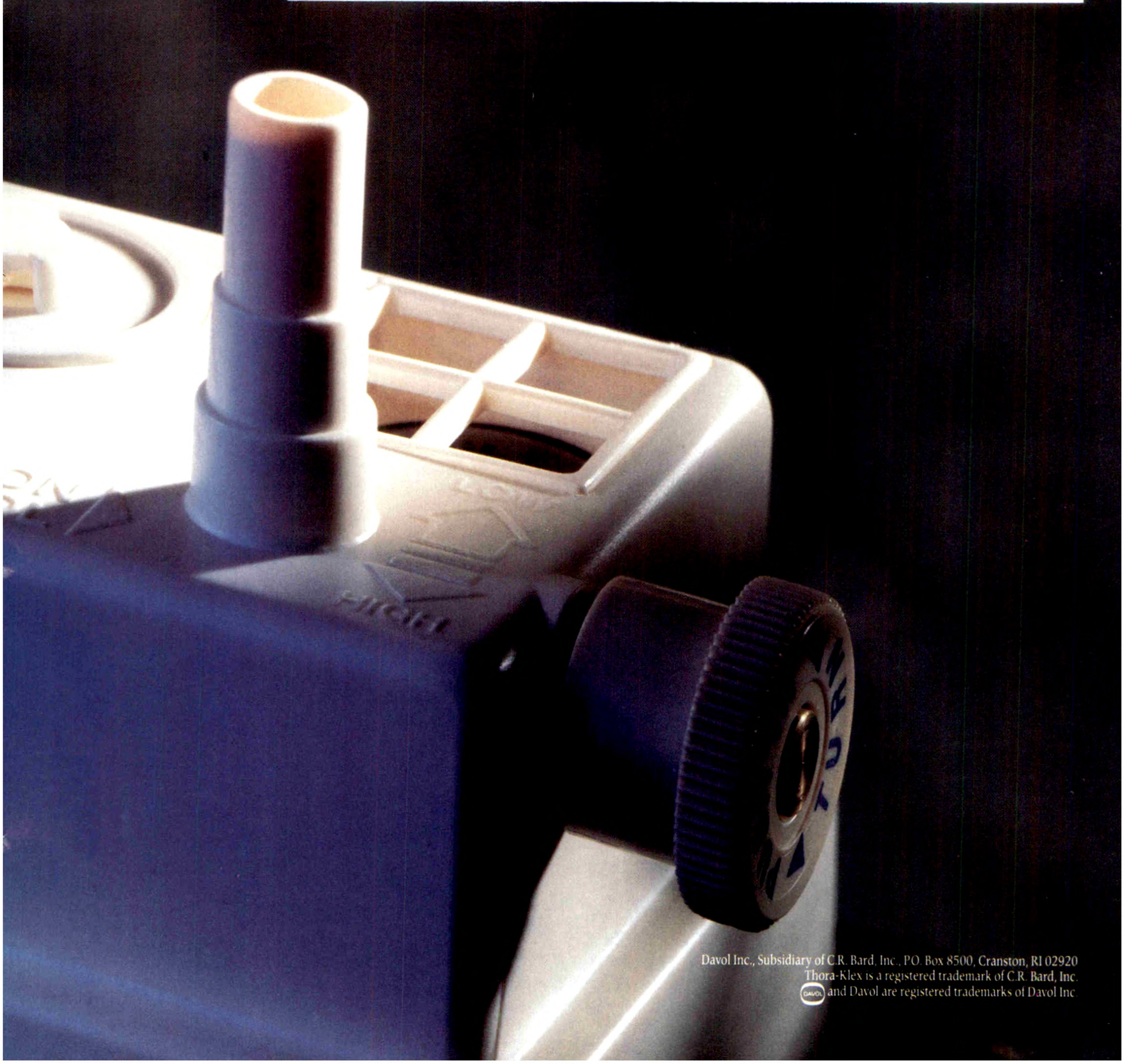

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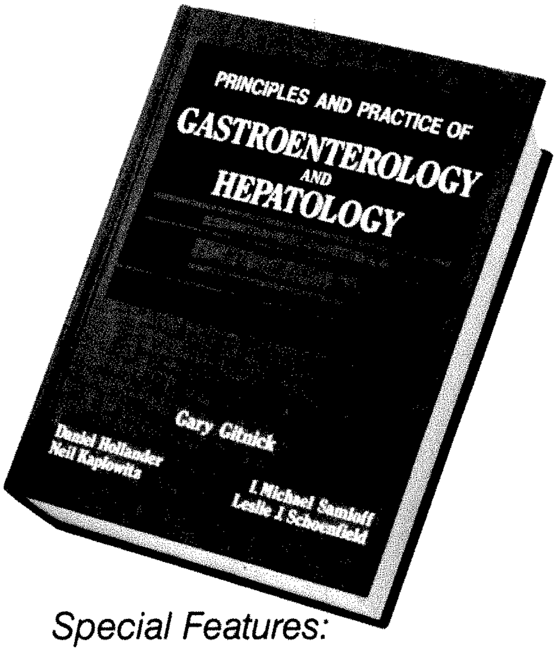

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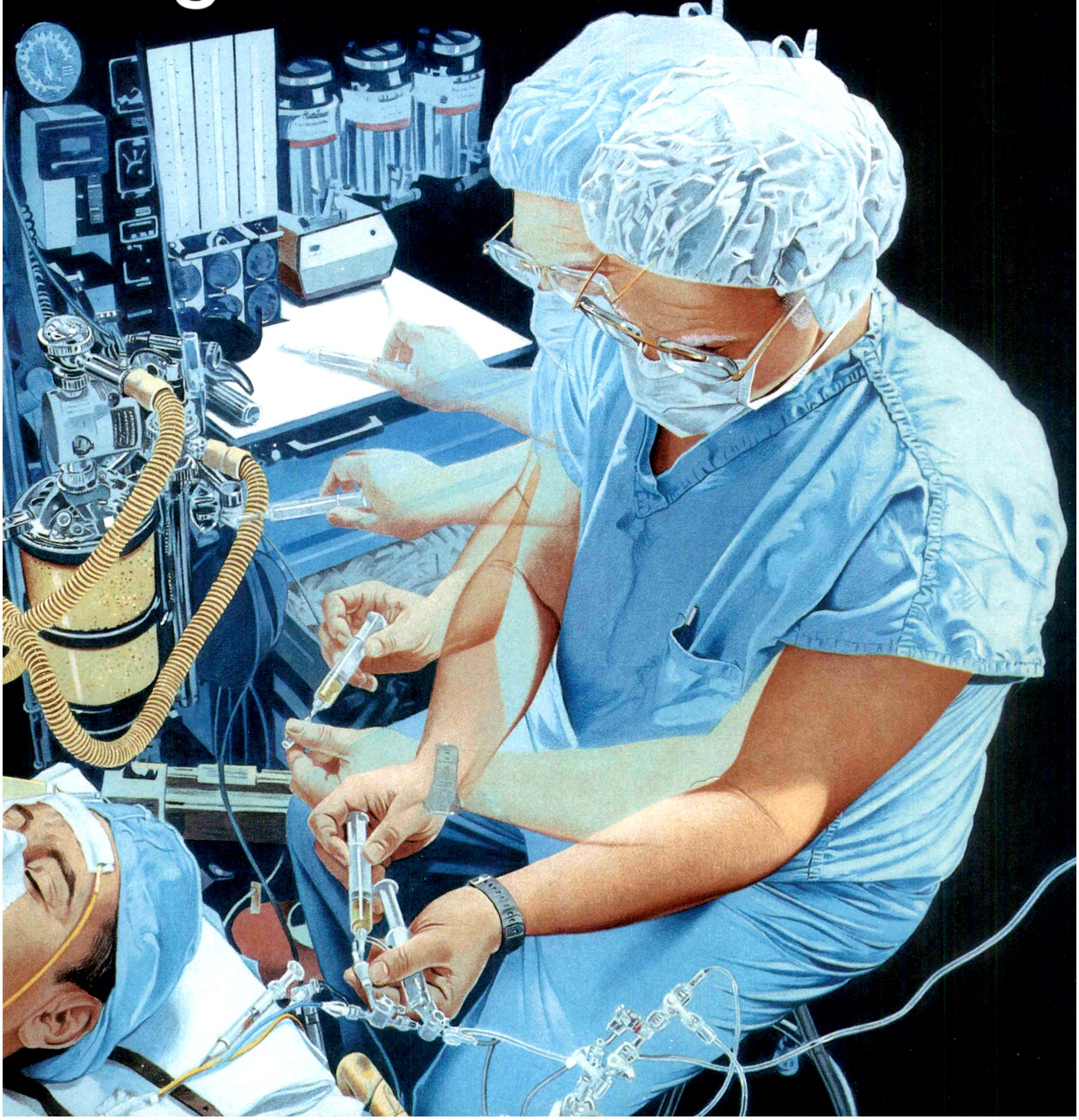
Compromised output, ischemia, and the highly vulnerable cardiac surgery patient...

The next crucial step: raising output without raising MVO_2



A crucial step i
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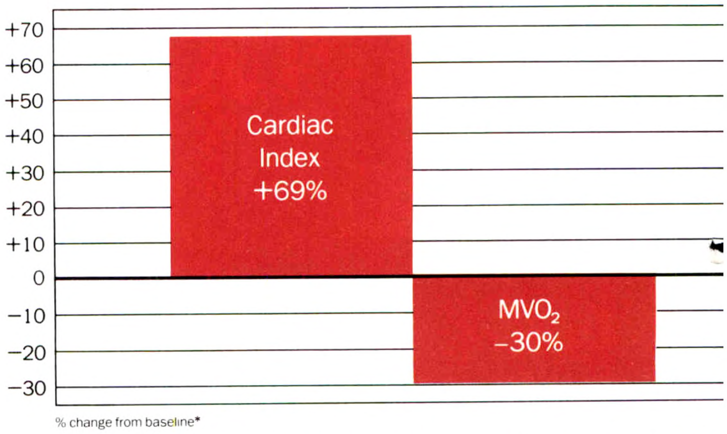
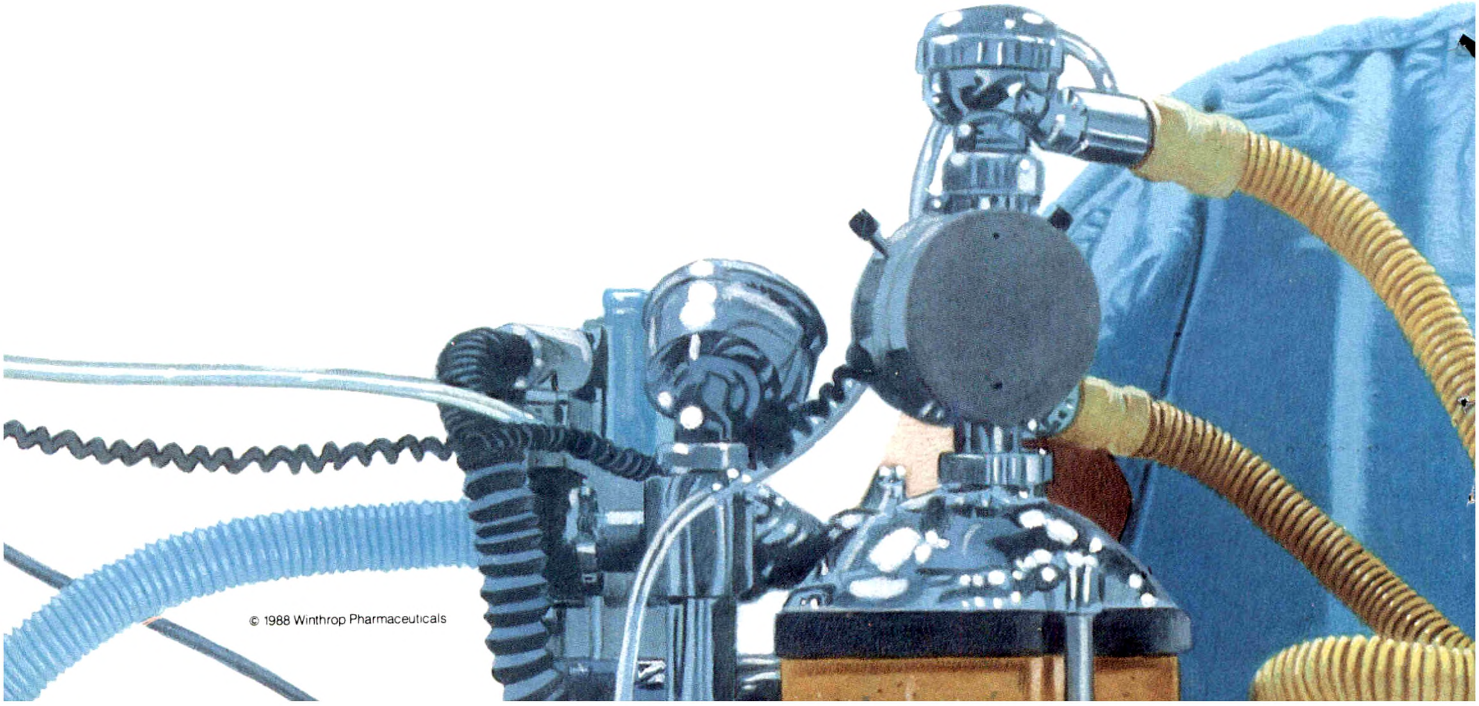
INOCOR I.V. (amrinone) provides improved hemodynamics without raising MVO_2 and worsening myocardial ischemia[1]



"...hemodynamic improvements with catecholamine agents such as dobutamine tend to be achieved only at the expense of a 30 to 40% increase in myocardial oxygen...."[2]

*n=8. Adapted from Benotti et al! Amrinone was infused in patients with severe congestive hear failure due to coronary artery disease at 2.5 mg/kg over 1 hour.

1. Benotti JR, Grossman W, Braunwald E, et al: Effects of amrinone on myocardial energy metabolism and hemodynamics in patients with severe congestive heart failure due to coronar artery disease. *Circulation* 1980;62:28–34.
2. Baim DS: Effects of amrinone on myocardial energetics in severe congestive heart failure. *Am J Cardiol* 1985;56:16B–18B.



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- Unique mechanism of action—PDE III inhibition
- Significantly improves pulmonary hemodynamics
- Efficacy maintained even in patients on beta blockers
- Does not increase the risk of arrhythmias (see Precautions)

Dual-acting, energy-efficient

Inocor® I.V.

(AMRINONE)

Raises output without raising MVO_2

Please see following page for important product information concerning contraindications, warnings, adverse reactions, patient selection, and prescribing and precautionary recommendations.

INOCOR I.V.:

Potent inotropic action in low output syndrome without increasing MVO_2 or aggravating myocardial ischemia

- A unique mode of action—selective PDE III inhibition
- No effect on platelet function
- No significant increase in risk of arrhythmias (see Precautions)
- Safe and effective when used concomitantly with intravenous or inhaled anesthetics
- Unlike catecholamines, does not act on the beta receptors—may be used effectively in patients on beta blockers

Brief Summary

Please consult full product information before prescribing. A summary follows.

INOCOR lactate injection, brand of amrinone lactate, represents a new class of cardiac inotropic agents with vasodilator activity, distinct from digitalis glycosides or catecholamines.

INDICATIONS AND USAGE INOCOR lactate injection is indicated for the short-term management of congestive heart failure. Because of limited experience and potential for serious adverse effects (see ADVERSE REACTIONS), INOCOR should be used only in patients who can be closely monitored and who have not responded adequately to digitalis, diuretics, and/or vasodilators. Although most patients have been studied hemodynamically for periods only up to 24 hours, some patients were studied for longer periods and demonstrated consistent hemodynamic and clinical effects. The duration of therapy should depend on patient responsiveness.

CONTRAINDICATIONS INOCOR lactate injection is contraindicated in patients who are hypersensitive to it. It is also contraindicated in those patients known to be hypersensitive to bisulfites.

PRECAUTIONS *General:* INOCOR lactate injection should not be used in patients with severe aortic or pulmonic valvular disease in lieu of surgical relief of the obstruction. Like other inotropic agents, it may aggravate outflow tract obstruction in hypertrophic subaortic stenosis.

During intravenous therapy with INOCOR lactate injection, blood pressure and heart rate should be monitored and the rate of infusion slowed or stopped in patients showing excessive decreases in blood pressure.

Patients who have received vigorous diuretic therapy may have insufficient cardiac filling pressure to respond adequately to INOCOR lactate injection, in which case cautious liberalization of fluid and electrolyte intake may be indicated.

Supraventricular and ventricular arrhythmias have been observed in the very high-risk population treated. While amrinone per se has not been shown to be arrhythmogenic, the potential for arrhythmia, present in congestive heart failure itself, may be increased by any drug or combination of drugs.

Thrombocytopenia and hepatotoxicity have been noted (see ADVERSE REACTIONS).

INOCOR is not recommended for use in acute myocardial infarction.

LABORATORY TESTS *Fluid and electrolytes:* Fluid and electrolyte changes and renal function should be carefully monitored during amrinone lactate therapy. Improvement in cardiac output with resultant diuresis may necessitate a reduction in the dose of diuretic. Potassium loss due to excessive diuresis may predispose digitalized patients to arrhythmias. Therefore, hypokalemia should be corrected by potassium supplementation in advance of or during amrinone use.

DRUG INTERACTIONS In a relatively limited experience, no untoward clinical manifestations have been observed in patients in whom INOCOR lactate injection was used concurrently with the following drugs: digitalis glycosides; lidocaine, quinidine; metoprolol, propranolol; hydralazine, prazosin; isosorbide dinitrate, nitroglycerine; chlorthalidone, ethacrynic acid, furosemide, hydrochlorothiazide, spironolactone; captopril; heparin, warfarin; potassium supplements; insulin; diazepam.

One case of excessive hypotension was reported when amrinone was used concurrently with disopyramide.

Until additional experience is available, concurrent administration with Norpace® (disopyramide) should be undertaken with caution.

CHEMICAL INTERACTIONS A chemical interaction occurs slowly over a 24-hour period when the intravenous solution of INOCOR lactate injection is mixed directly with dextrose (glucose)-containing solutions. **THEREFORE, INOCOR LACTATE INJECTION SHOULD NOT BE DILUTED WITH SOLUTIONS THAT CONTAIN DEXTROSE (GLUCOSE) PRIOR TO INJECTION.**

A chemical interaction occurs immediately, which is evidenced by the formation of a precipitate when furosemide is injected into an intravenous line of an infusion of amrinone. Therefore, furosemide should not be administered in intravenous lines containing amrinone.

USE IN PREGNANCY *Pregnancy category C:* There are no adequate and well-controlled studies in pregnant women. Amrinone should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

USE IN NURSING MOTHERS Caution should be exercised when amrinone is administered to nursing women, since it is not known whether it is excreted in human milk.

USE IN CHILDREN Safety and effectiveness in children have not been established.

ADVERSE REACTIONS *Thrombocytopenia:* Intravenous INOCOR lactate injection resulted in platelet count reductions to below 100,000/mm^3 or normal limits in 2.4% of patients.

Gastrointestinal effects: Gastrointestinal adverse reactions reported with INOCOR lactate injection during clinical use included nausea (1.7%), vomiting (0.9%), abdominal pain (0.4%), and anorexia (0.4%).

Cardiovascular effects: Cardiovascular adverse reactions reported with INOCOR lactate injection include arrhythmia (3%) and hypotension (1.3%).

Hepatic toxicity: In dogs, at IV doses between 9 mg/kg/day and 32 mg/kg/day, amrinone showed dose-related hepatotoxicity manifested either as enzyme elevation or hepatic cell necrosis or both. Hepatotoxicity has been observed in man following long-term oral dosing and has been observed, in a limited experience (0.2%), following IV administration of amrinone.

Hypersensitivity: There have been reports of several apparent hypersensitivity reactions in patients treated with oral amrinone for about two weeks. Signs and symptoms were variable but included pericarditis, pleuritis, and ascites (one case); myositis with interstitial shadowing on chest x-ray and elevated sedimentation rate (one case); and vasculitis with nodular pulmonary densities, hypoxemia, and jaundice (one case). The first patient died, not necessarily of the possible reaction, while the last two resolved with discontinuation of therapy. None of the cases were rechallenged, so attribution to amrinone is not certain, but possible hypersensitivity reactions should be considered in any patient maintained for a prolonged period on amrinone.

General: Additional adverse reactions observed in intravenous amrinone clinical studies include fever (0.9%), chest pain (0.2%), and burning at the site of injection (0.2%).

MANAGEMENT OF ADVERSE REACTIONS *Platelet count reductions:* Asymptomatic platelet count reduction (to less than 150,000/mm^3) may be reversed within one week of a decrease in drug dosage. Further, with no change in drug dosage, the count may stabilize at lower than predrug levels without any clinical sequelae. Predrug platelet counts and frequent platelet counts during therapy are recommended to assist in decisions regarding dosage modifications.

Should a platelet count less than 150,000/mm^3 occur, the following actions may be considered:

- Maintain total daily dose unchanged, since in some cases counts have either stabilized or returned to pretreatment levels.
- Decrease total daily dose.
- Discontinue amrinone if, in the clinical judgment of the physician, risk exceeds the potential benefit.

Gastrointestinal side effects: While gastrointestinal side effects were seen infrequently with IV therapy, should severe or debilitating ones occur, the physician may wish to reduce dosage or discontinue the drug based on the usual benefit-to-risk considerations.

Hepatic toxicity: In clinical experience to date with IV administration, hepatotoxicity has rarely been observed. If acute marked alterations in liver enzymes occur together with clinical symptoms, suggesting an idiosyncratic hypersensitivity reaction, amrinone therapy should be promptly discontinued.

If less than marked enzyme alterations occur without clinical symptoms, these nonspecific changes should be evaluated on an individual basis. The clinician may wish to continue amrinone, reduce dosage, or discontinue the drug based on the usual benefit-to-risk considerations.

OVERDOSAGE Doses of INOCOR lactate injection may produce hypotension because of its vasodilator effect. If this occurs, amrinone administration should be reduced or discontinued. No specific antidote is known, but general measures for circulatory support should be taken.

HOW SUPPLIED Ampuls of 20 mL sterile, clear yellow solution containing INOCOR 5 mg/mL, box of 5 (NDC 0024-0888-20). Each 1 mL contains INOCOR lactate equivalent to 5 mg base and 0.25 mg sodium metabisulfite in Water for Injection. The pH of INOCOR lactate injection is adjusted to a range of 3.2 to 4.0 with lactic acid or sodium hydroxide.

Protect INOCOR lactate ampuls from light. Ampul packaging is light resistant for protection during storage.

Store at room temperature.

NOTE: Parenteral drug products should be inspected visually and should not be used if particulate matter or discoloration is observed.

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Human Immunodeficiency Virus and the Patient Who Needs a Cardiac Operation

Robert W. M. Frater, MD

Albert Einstein College of Medicine and Montefiore Medical Center, Bronx, New York

Much media attention has been given to cardiac surgeons who have declared, or been thought to declare, that they will refuse to operate on patients with antibodies to the human immunodeficiency virus (HIV). Official bodies and groups not directly involved with the performance of operations on HIV–positive patients have expressed two views: (1) that physicians do not have a moral right to refuse to care for patients because they carry the HIV [1] and (2) that testing for the HIV can only be done with the consent of the patient [2]. It is appropriate for cardiac surgeons to examine these issues thoughtfully and carefully.

Cardiac Operations in Patients Testing Positive for the Human Immunodeficiency Virus

The questions that need to be answered in deciding whether or not to do a cardiac operation in an HIV–positive patient are:

1. What are the relative risks of the HIV–positive state and the cardiac disease for which operation is indicated?
2. Is the risk of cardiac operation worse in the HIV–positive patient?
3. Can a cardiac operation adversely affect the course of HIV infection?
4. What is the risk to the health care personnel of operating on patients infected with HIV?

We must distinguish between the carrier of the HIV with no acquired immunodeficiency syndrome (AIDS) stigmata and the patient with established AIDS.

Human Immunodeficiency Virus Carrier in Need of a Cardiac Operation

Current information derived from studies of small numbers of homosexual men without cardiac disease who have not had cardiopulmonary bypass and who acquired their infection from homosexual activity rather than drug addiction or transfusion suggests that 60% of HIV carriers will be free of AIDS at 5 years [3]. If the indication for cardiac operation is urgent (for example, endocarditis with a ruptured valve and cardiac failure, or left main coronary artery disease with unstable angina unresponsive to medical therapy), the short-term prognosis for the cardiac disease is worse, as far as we know, than for the HIV carrier state and it is, therefore, reasonable to operate.

Risk of Cardiac Operation in Human Immunodeficiency Virus Carriers

From our experience and anecdotal information from others, we have a suspicion that some HIV carriers may respond poorly to both antibiotic and surgical therapy for endocarditis, but this certainly does not apply to all such patients [4]. The minimum requirement for determining this is knowledge of the HIV status in a substantial series of patients undergoing cardiopulmonary bypass.

Course of the Human Immunodeficiency Virus Infection After Cardiopulmonary Bypass

Cardiopulmonary bypass has significant short-term effects on the immune system. Could this accelerate the transition from the HIV carrier state to AIDS? Again, information on the HIV status of a series of patients undergoing cardiopulmonary bypass is essential to determine the answer to this question. Only advance knowledge of the HIV status of these patients will make it possible ultimately to find the answers.

The Patient With Acquired Immunodeficiency Syndrome in Need of a Cardiac Operation

Is it reasonable to consider cardiopulmonary bypass in a patient who has the immune suppression of AIDS and, in addition, the opportunistic infections that are its hallmark? The suppression of immune function by cardiopulmonary bypass can only aggravate the risk.

Is there any possibility that the patient would escape fatal complications? Even if the operative mortality were acceptable the question would remain whether the difference that there might be in prognosis between AIDS and endocarditis justified the surgical attack on the endocarditis.

The Risk to the Health Care Worker

Health care workers have been shown to be infected by contaminated needle pricks, by prolonged contact between blood and chapped skin, and by buccal splashing [5]. The conversion rate from sharp instrument injuries is less than 1%. There is no denominator for the dermal and buccal cases and, therefore, no statement to be made on the level of hazard imposed by the accidents.

This is all the information we have from which to assess

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the risk to the participants in open cardiac operations. By extrapolation from the data on contaminated needle pricks, it is hoped that the risk will be low. However, there is no greater exposure to contaminated blood in clinical surgery, and all members of the team share the risks of multiple opportunities for sharp instrument injuries and splashing.

The extrapolation from previous health care worker experience to the special circumstances of open heart operations is a bold one. The risk needs to be studied.

Testing for the Human Immunodeficiency Virus

All of the foregoing discussion establishes that we do not have answers to the fundamental questions concerning the influence of HIV infection on the outcome of urgent cardiac operations and vice versa. Nor do we know the actual risk to the participants in the operation. It is clear that we cannot know without HIV testing of at least all patients believed to be at risk for carrying the virus.

Implications for an Individual of the Results of a Test for the Human Immunodeficiency Virus

If the test is positive, everything depends on whether the result is known by anyone other than the patient. A result recorded on a hospital chart or health service record is by definition no longer confidential. There are several possible consequences of a known positive result: work, health and life insurance, and lodging have all been denied known carriers of HIV. Even health care workers are at risk of losing employment. On the other hand, there is an absolute obligation to modify sexual behavior, to avoid procreation, and, in the case of drug addicts, to avoid needle sharing.

The Health Care Worker and the Right to Test

Knowledge of the HIV status of a patient is important to the health care worker prospectively: a known danger is always easier to handle than an unknown one. After a contaminating incident, knowledge of the HIV status of the patient is important whether it is positive or negative. For the health care worker who does acquire the HIV there is virtue in knowing the source.

Public Health and Human Immunodeficiency Virus Testing of Open Heart Surgical Patients

The HIV infection is the first transmissible disease in which testing for the infection has not been a right of those charged with investigating it, managing it, and attempting to control it. The societal, epidemiological, and individual advantages of knowing the patient's HIV status are unarguable. Set against these are the nonmedical hazards of a known HIV–positive status, which are recognized not only by special interest patient groups, but also by health care workers. If employer and societal attitudes could be changed and the potential for discrimination removed, there would be no problem. Until that takes place, confidentiality is important, whether the subject is being tested as part of a prospective study or during daily practice.

It is in fact not difficult to devise procedures whereby, when the patient so desires, absolute confidentiality can be preserved, and information only revealed to appropriate other parties: (1) if a contaminating incident occurs, (2) if the information could be useful in understanding and managing the subsequent clinical course of the patient, or (3) if the information could be valuable in retrospective analysis of a group of patients.

Ethics of Refusal to Operate in the Presence of Risk to the Operators

It has always been part of the ethic of our profession to give care despite personal risk. Physicians and nurses caring for patients with contagious disease and noncombatant medical first aid workers helping the injured on battlefields are obvious examples. There were always physicians who fled plagues [6], but during the recent brief halcyon time of the "pax antibiotica" a generation of health care workers has grown up believing itself safe from the risk of contagion. This belief was, of course, fallacious: hepatitis B infections, sometimes fatal, have been regularly acquired by surgeons over the last 35 years. The HIV has changed this complacency, not because it is especially contagious (it definitely is not), not because it is known to be a severe hazard during open cardiac operation on a carrier of HIV (no information is available on this risk), but because it is fatal once acquired. The stigma and publicity attached to the disease may, also, have influenced this fear.

It is possible to reduce the issue to simple terms. (1) The risk to the health care workers must be related to the worth of the procedure to the patient. It is possible that with more information a level of risk may be uncovered that, in relation to the benefit achieved for the patient, would make urgent open cardiac operation for the HIV–positive patient contraindicated. (2) We know the mechanism of infection. If there is no prolonged blood and skin contact, no blood and mucous membrane contact, and no puncture of the skin with a blood-contaminated sharp edge, there will be no infection. The issue, then, is to what extent these events can be controlled. It should be possible by discipline to eliminate all such incidents. To do this, surgical technique must change from the standard, and probably be slower than usual, and operations should not be done by inexperienced personnel. With what is currently known about the risk of needle prick injuries and the conversion rate of HIV carriers it is probably reasonable to perform open cardiac operations under strictly controlled conditions on HIV carriers who need an urgent cardiac operation and, therefore, it is probably unethical to refuse to operate.

At the same time, it is absolutely essential to have information on the HIV status of patients undergoing cardiopulmonary bypass to find out the risk of cardiopulmonary bypass for both patient and surgical team. Neither the medical nor the ethical question can be properly answered without the knowledge acquirable only by extensive testing for the HIV.

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Human Immunodeficiency Virus and the Cardiac Surgeon: A Survey of Attitudes

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The decision to operate on carriers of the human immunodeficiency virus (HIV) who need an urgent cardiac operation is difficult. There is a lack of knowledge about the effect of the presence of HIV on operative risk, about the effect of cardiopulmonary bypass on the progression of HIV infection to acquired immunodeficiency syndrome (AIDS), and about the risk to the cardiac surgical team of operating on 1 or more HIV carriers. This lack of knowledge is exacerbated by the strict regulations surrounding testing. We polled the board-certified cardiac surgeons in the United States on their willingness to perform open cardiac procedures on HIV carriers and AIDS patients. Fifty-three percent of the surgeons responded. Two thirds of them will operate on HIV carriers who need an urgent cardiac operation but regard the presence of AIDS as a contraindication to cardiopulmonary bypass. This is presumably a medical judgment. Those who will not operate on HIV carriers are apparently motivated by fear rather than moral judgments concerning the patients. Virtually all surgeons want to be able to test "high-risk" patients, and a substantial majority would test all patients.

(Ann Thorac Surg 1989;47:182–6)

There can be no doubt that open heart operations using cardiopulmonary bypass represent the largest routine exposure to blood that occurs in clinical medicine. The extensive use of sharp instruments, the large number of blood samples drawn, and the danger of splashing during cannulation and decannulation put surgeon assistants, scrub nurses, anesthetists, and pump technicians at risk to varying degrees.

Knowledge that blood-contaminated needle pricks and dermal and buccal exposure to blood have resulted in seroconversion, together with past experience of transmission of hepatitis viruses to surgeons, nurses, and others [1–6], has prompted some surgeons to refuse to operate on patients who test positive for antibodies to the human immunodeficiency virus (HIV). Some of these surgeons have described their attitudes to journalists and television reporters, and the print and electronic media have given these views considerable attention.

There are medical uncertainties about the patient with antibodies to HIV who needs a cardiac operation. Will the mortality associated with such operations be affected by infection with the virus? Will there be a difference in the response to operation between carriers of the virus and those who have the acquired immunodeficiency syndrome (AIDS) or the AIDS-related complex? Could cardiopulmonary bypass accelerate the progression from the carrier HIV-positive state to AIDS? Information on these questions is not yet published and has been made hard to get by the fact that it is generally necessary to obtain written and informed consent from the patient to test for the virus.

Although there is information on the risk of isolated needle prick injuries, there are no data on the real risk of participating in open heart operations.

The majority of HIV-positive patients who need cardiac operations are intravenous drug abusers, a few are homosexual or bisexual men, and only a small number have acquired the virus through no action of their own, that is, from transfused blood. Whether we like it or not, the attitudes of physicians to fellow citizens who are drug addicts or homosexuals may not be entirely objective.

Finally, there has been no disease in modern times that has been more politicized or received more attention than AIDS. Much has been published in peer-reviewed journals, but far more has appeared in the mass media.

Given this mixture of facts, uncertainties, fear, prejudices, and unprecedented publicity, we decided to poll cardiac surgeons in the United States on their attitudes toward performing open cardiac operations with cardiopulmonary bypass on patients whose blood contains the virus, and on whether testing for the virus should be freely allowed. This survey has been an independent effort of ours and has no connection with The Society of Thoracic Surgeons or any other corporate body.

Material and Methods

The questionnaire is shown in the Appendix. As pulmonary procedures for diagnostic purposes in patients with AIDS have been done by many cardiothoracic surgeons with no fanfare, we decided to concentrate on the subject that has caused most of the furor—open cardiac operations.

The 2 patients described in the first two questions presented the surgeon and the surgical team with the danger of HIV-containing blood. We assumed that most surgeons would recognize the first patient as almost

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certainly an addict, and the second is clearly depicted as having acquired the infection through no action of his or her own. A difference in the responses would indicate the exercise of moral judgment. The cases were deliberately made medically urgent so that there would be a clear difference between the prognosis as a result of the cardiac disease and the currently described average rate of progression from the HIV–positive state to AIDS–related complex or AIDS [7, 8].

The patients described in questions 3 and 4 present the same risk to the health worker and the same potential for moral judgments. However, they also pose the problems of a worse prognosis because of AIDS and the possibility of increased mortality from the operation.

Questions 5A and 5B raise the issue of compulsory testing for HIV. Do cardiac surgeons prefer to know the HIV status of a patient even though an operation properly conducted should present very little risk? Do they believe that it is possible to select "high-risk" patients for testing?

Finally, there are questions designed to get some idea of the frequency of exposure to HIV–positive patients, the risk of operation to the patient, and the risk of operation to health care personnel.

Although this may not have been necessary, the sensitivity surrounding the subject led us to make the survey anonymous. Thus, it was not possible to send individual follow-up letters to those who did not respond. With a response of more than 50%, we elected to analyze the answers we had rather than repeat the survey. The mailing list was purchased from The Society of Thoracic Surgeons. This list includes most of the board-certified cardiac surgeons in the United States but does not include some surgeons doing cardiac operations who have not joined The Society. Most of these are recent graduates who are not yet board-certified.

Of the somewhat fewer than 2,500 questionnaires sent out, there were 841 replies from surgeons currently performing cardiac operations and 235 replies from surgeons not doing cardiac operations. Nineteen were returned by the postal authorities as undeliverable. The recent report of the Ad Hoc Committee on Manpower of the American Association for Thoracic Surgery and The Society of Thoracic Surgeons [9] gave a number of 1,579 active cardiac surgeons. We believe, therefore, that with 841 replies, we have responses from more than half the active cardiac surgeons surveyed. The first 100 responses yielded the same proportions of answers as the total. Replies came from all zip code areas in the United States; a somewhat higher percentage of responses came from those areas with known high incidences of HIV infection.

Results

The responses from the 841 cardiac surgeons to part A of the first four questions are shown as percentages in Table 1. Two thirds of the responders will operate on the HIV carrier whatever the probable source of the infection, a quarter will not, and a few are uncertain. These figures are essentially reversed for the patient who has AIDS, but those who are uncertain are slightly more common. There is a small tendency to operate more frequently on the patient who has transfusion-acquired HIV infection whether or not AIDS has developed.

Table 1. Summary of Responses to Part A of First Four Questions[a]

Question	Yes	No	Uncertain
1	66	28	6
2	70	24	6
3	21	70	9
4	26	65	9

[a] Data are shown as percentages.

In response to the questions on required testing for HIV, more than 70% of surgeons want testing to be routine for all patients undergoing open heart operation and 95% want it for those considered to be at high risk for infection (Table 2). Fewer responders are uncertain about these questions.

The responses to questions 1B and 2B revealed a possible 227 HIV-positive patients who have had open heart operations. The responses to questions 3B and 4B revealed a possible 16 patients with AIDS who have undergone an open heart operation. Five responses to question 6 indicated that poor short-term results have been seen in these patients.

The responses to question 7 disclosed no new cases of HIV infection in health care workers.

There were many comments. These will be covered in the following section.

Comment

The answers to questions 1 and 2 show that a healthy majority of cardiac surgeons in the United States will perform urgent open heart procedures in patients infected with HIV, whether the virus was acquired iatrogenically or as the result of acts of the patient. A quarter of the surgeons, however, will not operate whatever the source of the infection.

The following two medical facts have contributed to these decisions. (1) An urgent need for an open cardiac procedure implies a shorter prognosis on average than is expected for a person found to have antibodies to HIV but no evidence of AIDS [3]. (2) By extrapolation from data on needle prick injuries and on dermal and buccal mucosal blood contact in health care workers, the risk of acquiring the infection is assumed to be low [1–6]. The risk of participation in a cardiac operation is simply not known.

The surgeons who will operate on HIV–positive pa-

Table 2. Summary of Responses to Questions About Required Testing for Human Immunodeficiency Virus[a]

Testing	Yes	No	Uncertain
All patients	73	24	3
High-risk patients only	95	3	2

[a] Data are shown as percentages.

tients presumably agree with the premise of the difference in prognoses, believe that they can control the risk by appropriate behavior and action, and, given these circumstances, are prepared to accept the risk of acquiring the infection even though the outcome is uniformly fatal.

The roughly 25% of surgeons who refuse to operate on the HIV–positive patients are for the most part also not influenced by the origin of the infection. It is possible that they are not impressed by the difference in the prognosis between the presence of antibodies to HIV and bacterial endocarditis or left main coronary disease demanding an urgent cardiac operation. It is also possible, and perhaps more likely, that they have looked at an unknown risk of acquiring a fatal disease in the course of performing an operation and decided that the level of the risk was less important than the fatal consequence. It is interesting to note that the very high contagiousness of hepatitis viruses, despite a quite low mortality, actually posed a similar risk of mortality per incident for health care workers, and yet apparently never caused any substantial number of cardiac surgeons to avoid operating on carriers of this particular virus. In general, the comments of the negative responders suggest the view that fear of infection is the major reason for refusal to operate.

Given the answers to questions 1 and 2, the reversal of responses to questions 3 and 4 must be due to a belief that the established immunodeficiency state defined by the presence of AIDS makes attempted lifesaving cardiac procedures either futile or excessively risky.

On the question of testing, three quarters of the responders want all patients tested, and 95% want all high-risk patients tested. Why would surgeons not be willing to confine mandatory testing to high-risk patients only? The answer, commonly expressed in the comments section of the questionnaire, is that without confession it is not always possible to know which patient is at high risk. That being so, why do all surgeons not insist on testing for all patients requiring cardiopulmonary bypass? The answer presumably is that some surgeons have a belief in patient autonomy, which they respect except in most unusual circumstances. It is striking, however, that surgeons who take the risk and also subject their helpers to that risk believe that patient autonomy is less important in this issue than do people who are not surgeons and who have analyzed the subject legally or theoretically [10, 11].

The answers to the questions on the numbers of HIV carriers and AIDS patients who have had cardiopulmonary bypass confirm that bypass has been used, but they cannot in any way be used to draw conclusions. The answers to question 6 reveal a suspicion that some HIV carriers may respond very poorly to antibiotic or surgical treatment of cardiac infections. The absence of a positive response to question 7 is modestly reassuring, although without statistical significance.

The comments section was used by 260 of the cardiac surgeons who responded. No statistical significance can be attached to these remarks. The most common views expressed were concern about the difficult issues that have been presented to cardiac surgeons by HIV, a hope that guidance can be offered, and a request to learn soon the results of the survey. A minority of the commentators expressed anger at official bodies that insist on an obligation to treat HIV–positive patients and indicated a concern for the safety of those in the operating room.

Finally, it is appropriate to discuss the importance of this survey. Our analysis is based on the view of 53% of the known board-certified cardiac surgeons in the United States. The respondents are from all geographical areas in this country. Most have not had direct experience in dealing with HIV carriers or AIDS patients needing cardiac operations. Although it is possible that the 47% who did not respond are a silent but substantial minority all with one view, it is unlikely that this is so. A survey with a response rate of 53% of the known board-certified cardiac surgeons probably reflects the attitudes of the specialty.

We are indebted to those members of The Society of Thoracic Surgeons who responded to the questionnaire.

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Appendix

Questionnaire Mailed to Members of The Society of Thoracic Surgeons in the United States

Do you currently perform open heart surgery?
________ Yes ________ No

1. Endocarditis, valvular insufficiency, urgent valve replacement needed in an HIV-positive patient (no AIDS-related complex, no AIDS).
   A. Will you operate? ________ Yes ________ No
   B. How many such cases have you done? ________
2. Left main, unstable angina, HIV-positive from a previous transfusion (no AIDS, no AIDS-related complex).
   A. Will you operate? ________ Yes ________ No
   B. How many such cases have you done? ________
3. Endocarditis, valvular insufficiency, urgent valve replacement needed in an HIV-positive patient with AIDS.
   A. Will you operate? ________ Yes ________ No
   B. How many such cases have you done? ________
4. Left main, unstable angina in a patient HIV-positive from a previous transfusion with AIDS.
   A. Will you operate? ________ Yes ________ No
   B. How many such cases have you done?
5. A. Should every patient coming for open heart surgery be required to be tested for HIV?
   ________Yes ________ No
   B. Should patients coming for open heart surgery who are at high risk for HIV infection be required to be tested? ________ Yes ________ No
6. Is there any evidence of a difference in short-term (say 90-day) results in an HIV-positive patient compared with an HIV-negative patient after open heart surgery? ________ Yes ________ No
7. Do YOU know of any HIV infection in health care workers that is related to working on a cardiac surgical case? ________ Yes ________ No

Your comments (optional): ______________________________
____
____

DISCUSSION

DR RONALD ABEL (Newark, NJ): As Mr Condit indicated, the point of departure for performing this survey was the recent media interest on this subject. Acquired immunodeficiency syndrome seems to be one subject on which everybody has an opinion and expresses it. If one reviews the past half year, there have been numerous articles in the lay press, in the *JAMA*, and in the *New England Journal of Medicine* written by ethicists, philosophers, historians, internists, and others who wave the flag of the importance of physicians caring for all patients under all circumstances. I think that those of us who toil in the operating room every day and have our hands immersed in blood may look at the situation a little bit less philosophically and a little bit more practically.

I have a couple of additional comments and two questions for the authors of the paper. Acquired immunodeficiency syndrome today, in 1988, is still primarily a bicoastal disease. We see it in New York, Los Angeles, San Francisco, Newark, and Miami, but basically it is not yet much of a problem in the heartland of the country. Follow-up questions in the survey below each surgeon's response asked how many cases each surgeon actually operated on in each category of HIV–positivity, yet those data were not presented this morning. I wonder how many of the surgeons who said that they *would* operate on an HIV–positive patient actually have been faced with that decision and have actually brought that patient to the operating room and subjected their surgical teams, perfusionists, and postoperative nurses to the risk of contagion.

In presenting a paper like this, it is very important in a public forum to look out for the press. The press is very, very interested in finding a physician as a target who would state that he would not operate on patients with AIDS. That's obviously not what this paper is about. As thoracic surgeons we have a genuine obligation to all patients, to care for everyone in need of our surgical care. There are, however, certain issues with regard to cardiopulmonary bypass that represent the cold, hard facts of exposure to blood versus the possible futility of surgical treatment, which Mr Condit outlined.

Finally, I wonder if you would comment on the role of the surgical assistants in making the decision. Some institutions have required that all nursing personnel and perfusionists must care for all patients under all circumstances under threat of termination of their employment if they refuse. Our making the decision based on our own philosophy or feelings is one thing, but dragging an entire team into that decision is a bigger responsibility, which I know that I feel.

DR QUENTIN STILES (Los Angeles, CA): It is important to air this subject in a public forum, but we must be careful to interpret our motives.

When a surgeon decides not to operate on a patient with AIDS or one who is HIV–positive, there are at least three possible factors underlying his decision-making process: (1) fear of transmission of the disease to himself and others on his team, (2) disapproval of a life-style, and (3) belief that the operation is contraindicated on a purely medical and scientific basis. This report does not clarify the thinking underlying the decisions of those who said they would not operate. Surgeons certainly modify their indications for specific cardiac operations when other factors are present. An example could be a patient with coronary disease who also has metastatic carcinoma.

I personally have faith in the courage and compassion of our medical profession, and in particular I believe that the great majority of thoracic surgeons in the country make their decisions about patient management based on what they think represents the best interests of their patients. The presence of a positive HIV status in a patient throws an enormous unknown factor into the risk-benefit calculation. We should continue to encourage widespread preoperative HIV testing of patients and health care workers so that we can learn more quickly about the added risk associated with a positive HIV status. Because of the current emotional climate regarding AIDS, confidentiality of test reports is essential to preserve the rights of the people being tested, but we as medical workers must be free to evaluate this disease as we do others.

DR SHLOMO GABBAY (Newark, NJ): In Newark, New Jersey, unfortunately we have a large population of HIV–positive patients admitted every day to our trauma center. In 1985 I replaced an infected aortic valve of a 33-year-old HIV–positive man with no documented AIDS. His white blood cell count before the operation was over 20,000/μL. Postoperatively the patient did well. On the sixth postoperative day, however, the patient developed severe respiratory deficiency and his white blood cell count went down to 300/μL. Full-blown AIDS developed and the patient died 33 days after operation. Our belief was that the cardiopulmonary bypass was probably an additional insult to his immune system.

Although we were dealing with only 1 patient, we were discouraged to continue to perform open heart operations on this kind of patient. Our early reluctance to perform major noncardiac operations on HIV–positive patients turned out to be unjustifiable, because the early results have been very good. We received every day HIV–positive patients with gunshot wounds and stab wounds who overcame major operations very well. The few patients who needed decortication had excellent results.

The real question is not if a surgeon can perform or wants to perform the operation but what kind of result we can expect. Maybe cardiopulmonary bypass will accelerate the appearance of AIDS. If so, why bother to do the operation? I would like to know from the authors if they have had some success with valve replacement on HIV–positive patients.

Hundreds of trauma patients positive for HIV are treated every day around the country and undergo major operations, and the results appear to be very good, but we need to know more about these results. We also have to understand more about the real risk to the surgeon, which, at least at this stage, I understand to be extremely low.

DR PHILIP SAWYER (Brooklyn, NY): Well, I have both a question and an answer. At the cocktail party before the Thoracic Society meeting in New York last fall, I had a knock-down-drag-out fight with Bob Frater about this issue. I insisted that we had a moral obligation to take care of these patients, and Bob squelched me like a flea with his final comment, which was, essentially, how do you justify operating on people with advanced AIDS who you know are going to be dead in 4 to 6 months? There is simply no cost-effective answer to that question. When you have a large population of patients with AIDS such as we have in New York and you know most of those patients aren't going to survive a substantial postoperative period, you really have to work very hard to justify the exposure of your operative team to that group of patients.

Also, however, we have another problem in the big cities where there are a lot of cases of AIDS. All of us who have had large practices for many years have a number of people with AIDS who have AIDS because of us. We have given them transfusions. They have come back with AIDS 4, 5, or 6 years later. They received the blood at a time when we didn't even know AIDS existed. The blood that was given them is permanently lodged in a freezer at the New York Heart Association's blood bank. We are told that that patient received blood that had HIV in it. They come back to you for help. I'd like to ask Dr Abel what he's going to do about that very substantial group of patients, which must be almost 5% to 7%, maybe even 10%, of our patients with HIV in New York City.

DR FRATER: Let me start by just rehearsing quickly why it is appropriate to offer operation to a person with the virus. If that person has a short-term threat to his life from cardiac disease, it is, I believe, appropriate. At the present time, based only on retrospective studies of homosexual men—and they may not be the same as other patients—the data show that 50% of patients infected with HIV develop AIDS by 10 years, and an additional 15% develop an AIDS-related complex. That means that there is a long potential prognosis for such patients. If the cardiac disease may kill them in a month, it is then appropriate to offer operation, accepting the fact that we do not really know whether cardiac operation, which does depress the immune system, will accelerate the progression to AIDS. We do not know for a simple reason: we haven't been able to develop the information because we haven't been able to test freely.

The very limited data that we have on patients known preoperatively to be HIV positive show that—and this is a series of only 11 such operations (all operations for endocarditis) in which we knew in advance the HIV status—if they had uncontrolled infection at the time of operation (and we all know that one of the indications for cardiac operation in endocarditis is failure to control the infection), the mortality was extremely high. The patients went on to die of unremitting sepsis even while we were continuing the postoperative antibiotic course. On the other hand, in the 4 patients in whom the infection had been controlled preoperatively, we found that 3 of them did very well; one came down with AIDS 3.5 months later and died rather rapidly.

That is not enough information to make a decision. We do not know the effect of cardiopulmonary bypass on progression to AIDS. Obviously this is a potential risk. We do think that if we had a patient with life-threatening cardiac disease and no active infection but carrying the HIV, it would be reasonable to offer that patient operation based on the differential prognosis between an HIV–carrier state (non-AIDS) and the prognosis of his disease.

Now, let me try to answer the specific questions. We did not report the questions on how many of you have had experience with HIV–positive patients. There were some 200 apparent cases that had been done, but we had no way of knowing, as we had run our survey anonymously, whether there was duplication of information, and we didn't regard it as sufficiently reliable information to be worth reporting.

On the question of dragging your team into the operation, I think a team is a team, and the whole team must work together. We did this by bringing our team together and having a number of debates. Finally, in December 1984 (having treated, I'm sure, many patients without knowing what we were doing), we were suddenly confronted with, of all things, a bisexual heroin addict who had an HIV–positive test. The team agreed to operate and the team has agreed since. I think you just have to insist on that. I honestly don't think you can make this a voluntary effort.

Dr Stiles raised some extremely important questions, which we have deliberately avoided here. What do you do with a recidivist drug addict? I think whether that person is HIV positive or not, even if he's HIV negative, if he's a recidivist drug addict we can raise a whole set of issues that would take us another day to debate, and I don't really think we should answer that.

I think I've answered the question on the left main with metastatic carcinoma by pointing out that the prognosis for an HIV–positive state is such that we probably are obliged to operate. I dare say the prognosis of an HIV–positive state may be better than that of metastatic carcinoma.

There's no question that we don't know enough about the disease and we will only know if we have universal testing. There are enormous difficulties in demanding testing. People who are known to be HIV positive have lost their health insurance, their life insurance, and their housing. They've had their houses burned down around them, and they have lost their employment. Physicians and health care workers have, unfortunately, been dismissed by their own hospitals when found out to be HIV positive.

With those kinds of both stigmata and practical disadvantages to being HIV positive, it is not surprising that people don't want the results known. It is obvious that we must have a confidential system of testing, and it's easily possible to devise that. Obviously I don't have the time to discuss that.

Reperfusion Injury in the Lung Preserved for 24 Hours

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The left lower lobes of 28 canine lungs were isolated, preserved, and then reperfused for 150 minutes. Five groups of lobes were studied: group 1, control (n = 5); group 2, one hour of warm ischemia (n = 5); group 3, one hour of warm ischemia + oxygen free radical scavengers (n = 5); group 4, 24 hours of cold ischemia (n = 8); and group 5, 24 hours of cold ischemia + oxygen free radical scavengers (n = 5). Oxygen free radical scavengers consisted of superoxide dismutase and catalase (100 μg/mL) given at the moment of reflow. Extravascular lung water (grams per gram of blood-free dry lobe weight) after reperfusion was 2.75 ± 0.19, 5.46 ± 0.60, 4.08 ± 0.37, 9.43 ± 0.98, and 6.91 ± 0.95 for groups 1 through 5, respectively ($p < 0.05$, groups 2 through 5 versus group 1; $p < 0.05$, group 2 versus group 3 and group 4 versus group 5). Lung tissue lipid peroxidation, measured as thiobarbituric acid reactive material, was 117 ± 14, 314 ± 19, and 163 ± 25 nmol/g dry lobe weight for groups 1, 4, and 5, respectively ($p < 0.05$, group 4 versus group 1 and group 4 versus group 5). The data suggest that oxygen free radical scavengers attenuate reperfusion injury after long-term hypothermic lung preservation.

(Ann Thorac Surg 1989;47:187–92)

Current methods of lung preservation for transplantation generally employ metabolic inhibition with a cold Collins' solution flush followed by hypothermic storage [1]. Despite reported lung function and occasional survival in laboratory animals after 24-hour lung preservation and transplantation, the acceptable "safe" period for clinical lung transplantation remains about four hours of cold preservation [2, 3]. Room for new approaches to improve lung preservation appears to exist [3].

It is now apparent that the lung, like many other tissues, suffers an injury associated with reperfusion following an ischemic period and mediated by oxygen free radicals. Oxygen free radical scavengers (OFRS) ameliorate lung injury after short-term warm ischemia [4]. The purpose of this study was to establish a reliable model to study reperfusion injury after long-term hypothermic lung preservation and to assess the ability of OFRS to reduce any such injury.

Material and Methods

Twenty-eight heartworm-free dogs were anesthetized with sodium pentobarbital, 0.5 mL per kilogram of body weight administered intravenously, and intubated. All animals received humane care in compliance with the "Guide for the Care and Use of Laboratory Animals" (NIH Publication No. 85-23, revised 1985), and the study was approved by the institutional animal care and use committee (ID 87-457). A left thoracotomy and left upper lobectomy were performed, and 10,000 units of heparin sodium was administered intravenously. Blood (450 mL) was withdrawn from a femoral arterial line and stored in citrate-phosphate-dextrose. A No. 24 cannula (USCI, Glens Falls, NY) was positioned in the left lower lobar vein, a No. 14 cannula was secured in the left lower lobar artery, a No. 5.5 endotracheal tube was placed in the left lower lobar bronchus, and the isolated left lower lobe was removed from the thoracic cavity.

Five groups of isolated lobes were established. Group 1 (n = 5) served as controls and underwent immediate perfusion without intervening ischemia. Groups 2 (n = 5) and 3 (n = 5) were flushed at low pressure (less than 20 mm Hg) with 500 mL of Ringer's lactate and maintained in the deflated state at room temperature for one hour before reperfusion. Flush pressure was continuously monitored by a small catheter within the lumen of the arterial cannula attached to a pressure transducer. Groups 4 (n = 8) and 5 (n = 5) were flushed with 500 mL of cold modified Collins-Sacks solution [2], inflated, submerged, and stored at 4°C for 24 hours.

After the variable preservation period, all 28 isolated lobes underwent an identical 150-minute reperfusion. Arterial and venous cannulas were connected to a $\frac{3}{16}$-inch Tygon tubing circuit containing a reservoir primed with the previously collected autologous blood (Fig 1). Perfusate was pumped continuously by a model 5050 Sarns pump (Ann Arbor, MI) and maintained at 37°C by a Travenol heat exchanger. Small catheters within the lumen of the arterial, venous, and bronchial cannulas, connected to Statham P23Db pressure transducers and a model 1308A Hewlett-Packard recorder, provided continuous monitoring of pulmonary arterial pressure, pulmonary venous pressure, and airway pressure. Flow rate was measured with an EP 300 electromagnetic flow probe

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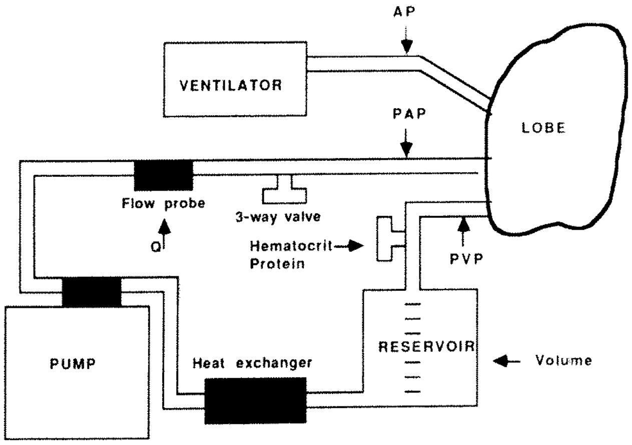

Fig 1. Isolated perfused canine left lower lobe preparation. Reperfusion period was 150 minutes at a flow rate (Q) of 176 ± 2 mL/min and a pulmonary venous pressure (PVP) *of 0 mm Hg. Lobes were ventilated at a tidal volume of 150 mL at six cycles per minute.* (AP *= airway pressure;* PAP *= pulmonary arterial pressure.)*

(Carolina Medical Electronics, King, NC). Pulmonary venous pressure was set at 0 mm Hg by adjusting the height of the venous reservoir. Flow rate was maintained constant at 176 ± 2 mL/min. Pulmonary vascular resistance (PVR) was calculated as pulmonary artery pressure/flow rate (millimeters of mercury per liter per minute). All lobes were ventilated with room air at a tidal volume of 150 mL and a rate of 6 cycles per minute.

Perfusate hematocrit and protein content, the latter measured by the biuret method, were recorded. The circulating volume was calculated by adding 0.2 mL of Cardio-Green (indocyanine green) dye (Fluka Chemical Co, Ronkonkoma, NY) to the reservoir, centrifuging a perfusate sample, reading against a plasma blank at 806 nm on a model DU 6 Beckman spectrophotometer, and comparing with a standard dilution curve. At the moment of reflow, 100 μg/mL of bovine erythrocyte superoxide dismutase (3,000 U/mg) and 100 μg/mL of bovine liver catalase (2,800 U/mg) (Sigma Chemical Co, St. Louis, MO), these constituting the OFRS, were added to the venous reservoir for the lobes of groups 3 and 5.

After the reperfusion period, extravascular lung water was determined by the method of Drake and associates [5]. Reperfused lobes were weighed and homogenized in a blender with 200 mL of water, and the weight of 0.2 mL of homogenate (Wh) was recorded. The absorbance at 540 nm of 0.2 mL of homogenate (Ah) and 0.02 mL of perfusate blood (Ab) in 5 mL of Drabkin solution was read. The lobes and 10 mL of perfusate blood were dried to a constant weight (Dl). The wet/dry weight ratio of the blood was calculated (R). From these data, the fraction of blood in the lobes (F) and the ratio of extravascular lung water to blood-free dry lobe weight (Qwl/dQl) were determined from the formulas:

$$
\begin{aligned}
F &= [0.02 \times Ah \times (Wl + 200)]/(Wl \times Wh \times Ab),\\
W &= (1 - F) \times Wl,\\
D &= Dl - [F \times (Wl/R)], \text{ and}\\
Qwl/dQl &= (W - D)/D,
\end{aligned}
$$

where Wl = weight of reperfused lobe, W = blood-free wet weight of the lobe, and D = blood-free dry weight of the lobe.

Lung tissue lipid peroxidation was measured as thiobarbituric acid (TBA) reactive material [6]. The assay was performed immediately after the 150-minute reperfusion of groups 4 and 5 left lower lobes. Controls consisted of the normal, nonischemic left upper lobe removed from the same animal. Groups 1 through 3 were not subjected to TBA assay. A 1-g specimen was homogenized in a Broeck tissue grinder in 9 mL of cold 1.5% potassium chloride to yield a 10% homogenate. Then 0.2 mL of homogenate was added to 0.2 mL of 8.1% sodium dodecyl sulfate, 1.5 mL of 20% acetic acid (pH 3.5), and 1.5 mL of 0.8% TBA. The mixture was made up to 4 mL with distilled water, heated at 95°C for 60 minutes, and then cooled. One milliliter of water and 5 mL of butanol/pyridine (15:1, vol/vol) were added. The solution was centrifuged at 4,000 rpm for ten minutes. The fluorescent intensity of the top layer was read in an Aminco-Bowman spectrophotofluorometer, excitation 515 nm and emission 553 nm. The lipoperoxide concentration (nmol/g) was determined by reference to a standard curve created with 0.3, 0.5, and 1.0 nmol of 1,1,3,3-tetramethoxypropane (Sigma).

Biopsy specimens of all the reperfused lobes were fixed in formalin and stained with hematoxylin and eosin. Interstitial and alveolar edema, atelectasis, vascular congestion, and red cell extravasation were graded as follows: 1 = minimal, 2 = moderate, and 3 = severe. Scores were added, and a histological injury index was calculated for each reperfused lobe.

Data between lobe groups were compared using the Mann-Whitney U nonparametric test. A *p* value of less than 0.05 was considered significant.

Results

All five groups of lobes were comparable in initial perfusate hematocrit, protein content, circulating volume, duration of reperfusion period, flow rate (176 ± 2 mL/min), venous pressure (0 mm Hg), arterial pressure, and peak airway pressure (Table 1).

During reperfusion, control lobes and lobes subjected to one hour of warm ischemia demonstrated a fall in PVR. Lobes preserved for 24 hours maintained a higher PVR (Fig 2). The addition of OFRS to the perfusate did not offer any advantage in terms of a lower PVR in the 24-hour–preserved, reperfused lobes (see Fig 2).

Final lobe weight, lobe/dog weight ratio, blood-free wet weight, and Qwl/dQl were all higher for lobes subjected to one hour of warm or 24 hours of cold ischemia compared with controls (Table 2). The addition of OFRS to the perfusate reduced edema formation during reperfusion after both one hour of warm and 24 hours of cold ischemia (group 2 versus group 3, group 4 versus group 5) (see Table 2). The protection against pulmonary edema afforded by OFRS did not appear to be secondary to hydrostatic changes because groups 2 and 3 and groups 4 and 5 had similar hemodynamic profiles during reperfusion (see Table 1, Fig 2).

Table 1. Standardized Reperfusion Variables of Preserved Lobes[a]

	Group				
Variable	1 (n = 5)	2 (n = 5)	3 (n = 5)	4 (n = 8)	5 (n = 5)
Hematocrit	34 ± 2	31 ± 3	32 ± 2	37 ± 2	36 ± 3
Protein (g/dL)	4.6 ± 0.4	4.3 ± 0.1	4.7 ± 0.2	5.1 ± 0.2	5.1 ± 0.3
Volume (mL)	505 ± 5	494 ± 5	508 ± 4	491 ± 3	495 ± 6
Duration (min)	150 ± 3	147 ± 12	150 ± 0	150 ± 6	150 ± 0
Pulmonary arterial pressure (mm Hg)	12.0 ± 2.6	12.5 ± 4.7	9.1 ± 0.9	11.4 ± 1.2	11.4 ± 2.7
Peak airway pressure (mm Hg)	12.2 ± 0.5	13.4 ± 1.5	12.9 ± 0.8	13.8 ± 0.7	12.8 ± 0.7

[a] Data are shown as the mean ± the standard error of the mean. Data were recorded at a constant flow rate of 176 ± 2 mL/min; pulmonary venous pressure, 0 mm Hg. p = not significant for groups 2 through 5 versus group 1 (Mann-Whitney U test).

After flush and 24-hour preservation but before reperfusion, lobes in groups 4 and 5 had an average weight of 82 ± 4 g (p = not significant, group 4 versus group 5). During subsequent reperfusion, group 4 had an 80% increase in weight to 149 ± 12 g, compared with only a 26% increase to 104 ± 12 g for OFRS-treated group 5 lobes ($p < 0.05$) (see Table 2).

Reperfused 24-hour–preserved lobes had increased lipid peroxidation, measured as TBA reactive material, compared with controls. The addition of OFRS reduced lipid peroxidation significantly during reperfusion (Fig 3). Final TBA reactive material levels were 39 ± 4 and 24 ± 2 nmol/g final wet lobe weight for groups 4 and 5, respectively ($p < 0.05$). When TBA reactive material was expressed as nanomoles per gram of dry lobe weight, the values were 314 ± 19 and 163 ± 25 for groups 4 and 5, respectively ($p < 0.05$). Nonpreserved, nonreperfused left upper lobes had TBA reactive material levels of 117 ± 14 nmol/g dry lobe weight ($p < 0.05$ versus group 4; p = not significant versus group 5).

The histological injury index was 5.6 ± 0.2, 9.6 ± 0.8, and 7.2 ± 0.9 for groups 1, 4 and 5 ($p < 0.05$, group 4 versus group 5; $p < 0.05$, group 1 versus groups 4 and 5). There was a linear correlation between the histological damage observed microscopically and that measured as extravascular lung water (Qwl/dQl) ($r = 0.97$, $p < 0.01$). Pulmonary architecture was better preserved in group 5 OFRS-treated, 24-hour preserved lobes than in lobes not receiving OFRS (Fig 4).

Comment

Current lung preservation for transplantation utilizes metabolic inhibition, flushing the pulmonary vasculature with a solution of an intracellular composition and storing the lung at low temperature. Using the same modified Collins-Sacks solution as in the present study, Crane and associates [2] reported survival in several dogs receiving a left lung transplant preserved for 24 hours. Metabolic maintenance techniques have been added to metabolic inhibition in an effort to extend tolerable experimental lung preservation. Toledo-Pereyra and co-workers [7] reported in vitro lung viability after 24 hours of hypothermic pulsatile perfusion. Despite these encouraging laboratory results, the upper limit for successful preservation of the excised lung for clinical transplantation utilizing hypothermic techniques is about four hours [3]. This study demonstrates a different approach to hypothermic lung preservation, the addition of OFRS at reflow. The method is simple, is easily applied clinically, and appears effective in reducing reperfusion-related edema formation after long-term lung preservation.

Evidence is increasing that the lung suffers a reperfusion injury after short periods of warm ischemia. Isolated rabbit lungs subjected to four hours of warm ischemia rapidly develop edema on reperfusion, with an increase in oxygen free radical formation, all of which is prevented by superoxide dismutase [4]. Lodoxamide, a xanthine oxidase inhibitor that reduces formation of superoxide anion, prevents albumin leakage into reperfused isolated rat lungs after two hours of warm ischemia [8]. These data suggest that a similar reperfusion injury might be possible after long-term hypothermic lung preservation.

The present model demonstrates an oxygen free radical–mediated injury after reperfusion of the lung preserved for 24 hours. Reperfusion of the preserved lung was associated with increases in extravascular lung water, PVR, lipid peroxidation, and histological deterioration compared with normal lung controls. The addition of 100 μg/mL of OFRS at reflow, a dosage used successfully in previous isolated perfused lung preparations [9], reduced

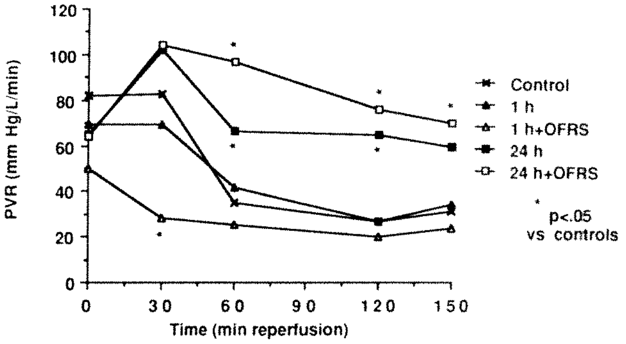

Fig 2. Pulmonary vascular resistance (PVR) *during reperfusion of preserved lobes.* (OFRS = *oxygen free radical scavengers [addition of 100 μg/mL superoxide dismutase and catalase at reflow].*)

Table 2. Extravascular Lung Water After Reperfusion of Preserved Lobes[a]

	Group				
Variable	1	2	3	4	5
Dog weight (kg)	21 ± 1	19 ± 1	23 ± 2	20 ± 1	20 ± 2
Final lobe weight (g)	77 ± 8	112 ± 12^{b}	70 ± 7^{c}	149 ± 12^{b}	104 ± 12^{d}
Lobe/dog weight ratio (g/kg)	3.63 ± 0.20	5.93 ± 0.58^{b}	3.05 ± 0.27^{c}	7.70 ± 0.64^{b}	5.39 ± 0.89^{b,d}
Blood-free wet lobe weight (g)	52 ± 5	80 ± 13	51 ± 6^{c}	116 ± 11^{b}	80 ± 10^{b,d}
Blood-free dry lobe weight (g)	14 ± 1	12 ± 2	10 ± 1^{b}	13 ± 2	11 ± 2
Qwl/dQl	2.75 ± 0.19	5.46 ± 0.60^{b}	4.08 ± 0.37^{c}	9.43 ± 0.98^{b}	6.91 ± 0.95^{b,d}

[a] Data are shown as the mean ± the standard error of the mean. [b] $p < 0.05$ versus controls (Mann-Whitney *U* test). [c] $p < 0.05$ versus group 2. [d] $p < 0.05$ versus group 4 (Mann-Whitney U test).

Qwl/dQl = extravascular lung water (grams per gram of blood-free dry weight).

edema formation and lipid peroxidation in the lung preserved for 24 hours. Oxygen free radical scavengers also prevented pulmonary edema in the lung subjected to one hour of warm, deflated ischemia, a finding in agreement with previous studies [4]. The apparent reduction of edema provided by OFRS did not appear to be due to differences in hydrostatic or oncotic pressures between groups. Groups 4 and 5 had similar perfusate protein content and pulmonary arterial pressure throughout the reperfusion period. It would appear that the reperfused, 24-hour–preserved lung has an increased capillary permeability that can be improved with OFRS treatment.

Oxygen free radical scavengers did not prevent an increased PVR in 24-hour–preserved lobes during reperfusion and yet did reduce edema formation. At least in the present model of the 24-hour–preserved lobe, the OFRS reduction in edema is not mediated by a reduction in hydrostatic pulmonary pressure. Rather, it appears that OFRS reduce a capillary permeability "leak" that occurs in the 24-hour–preserved, reperfused lobe. Oxygen free radical scavengers may prevent endothelial cell damage by oxygen free radicals. In other studies of isolated perfused lungs, OFRS have reduced PVR after ischemia, presumably by reducing thromboxane production from damaged endothelial cells [10, 11]. However, these studies involved shorter periods of ischemia. Indeed, in the present study, group 3 lobes, subjected to brief warm ischemia and OFRS treatment, demonstrated a reduction in PVR (see Fig 2).

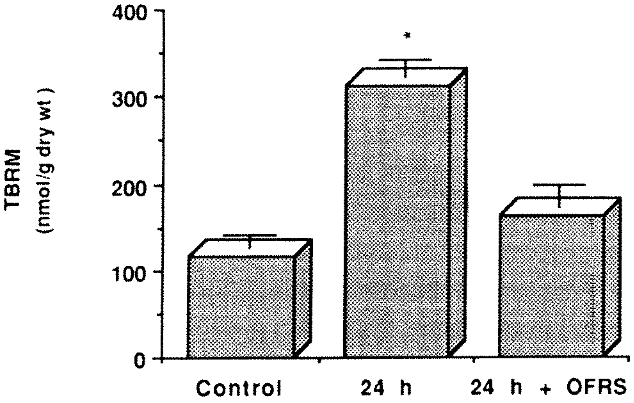

*Fig 3. Thiobarbituric acid reactive material (TBRM) in reperfused preserved lobes. (*p < 0.05 for 24 h versus control and 24 h versus 24 h + oxygen free radical scavengers [OFRS].)*

The majority of lung edema formation in this model occurred during reperfusion rather than during the preservation process. The average weight of flushed, 24-hour–submerged lobes of 82 ± 4 g is only slightly higher than that of control lobes, 77 ± 8 g. Oxygen free radical scavengers, given at the moment of reflow, were able to reduce the large increases in extravascular lung water during reperfusion of the lobe preserved for 24 hours.

After reperfusion of ischemic tissue, oxygen free radicals are generated from at least two sources: xanthine oxidase and neutrophils [11]. The hydroxyl radical, the most reactive species formed, can initiate a chain reaction of lipid peroxidation in endothelial cellular membranes that leads ultimately to altered permeability and edema [9, 12]. Pulmonary endothelial cell function, measured as serotonin uptake, is reduced by oxygen free radical generation, and OFRS prevent the deterioration [13].

Some authors have expressed reservations about the use of large molecules such as superoxide dismutase and catalase as scavengers because of their poor penetration into the endothelial cell. Several observations, however, may explain the effectiveness of superoxide dismutase and catalase in preventing lung reperfusion injury. First, an important injury appears to occur to the cellular membrane [9, 12, 13]. Second, normally the lung appears to contain extracellular superoxide dismutase [14]. Finally, superoxide dismutase and catalase, given at reflow, have repeatedly and successfully prevented reperfusion injury in a wide variety of organs [15]. The results of the present study lend support to a reperfusion injury in the lung preserved for transplantation. Reperfusion could lead to hydroxyl radical formation, lipid peroxidation of the pulmonary endothelial membrane, increased permeability, and pulmonary edema (Fig 5).

This study has several limitations. It is not known whether these in vitro results and relationships will be seen in an in vivo lung transplantation model. Although the extravascular lung water differences between OFRS–treated and untreated lobes in the face of similar perfusion pressures strongly suggest an alteration in pulmonary capillary permeability, the evidence is indirect.

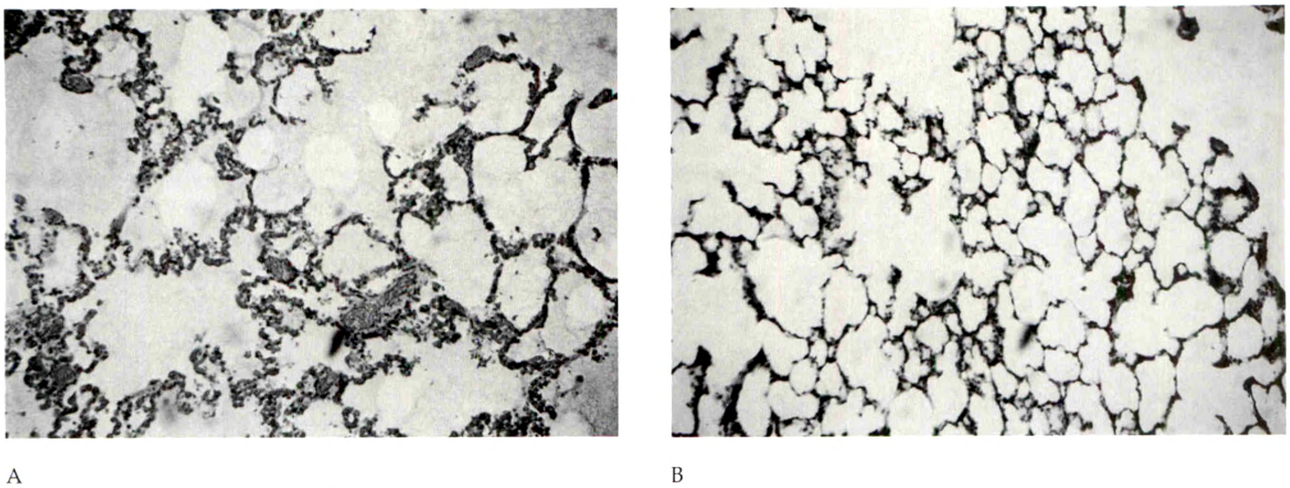

Fig 4. (A) Lung after 24 hours of cold preservation in a modified Collins-Sacks solution and reperfusion with blood for 150 minutes. There is marked vascular congestion, red cell extravasation, and alveolar edema. (B) Lobe treated in identical fashion to that in (A) except that 100 μg/mL of superoxide dismutase and catalase was given during reperfusion. Pulmonary architecture was preserved.

A more direct measure might employ the isogravimetric technique to determine the capillary permeability coefficient [16]. In the present model, it would have been exceedingly difficult to obtain an isogravimetric state at any reasonable flow rate and pulmonary pressure, as the lobes preserved for 24 hours continuously gained weight. The major advantage of the TBA assay is simplicity and sensitivity. It measures lipid peroxidation and is only a nonspecific, indirect measure of presumed hydroxyl radical activity. Electron spin resonance spectroscopy is replacing this technique [17].

Although OFRS significantly reduced edema formation in the lobe preserved for 24 hours, PVR was still elevated compared with control lobes. The unilaterally transplanted lung will require a near-normal PVR to be effective. Contralateral lung disease will require that the transplanted lung tolerate normal or even increased flow rates without further elevation in pulmonary arterial pressure and consequent right ventricular failure [18]. Although OFRS significantly reduced edema formation, the treated lobes still had higher extravascular lung water than control perfused lobes, implying that there is at least a component of the injury that is not related to free radical production. One could argue that preservation and reperfusion of a single lobe is not analogous to that of an entire lung. However, a recent study employing an entire heart-lung block showed that allopurinol or catalase reduced edema in 24-hour–preserved, reperfused whole lungs [19].

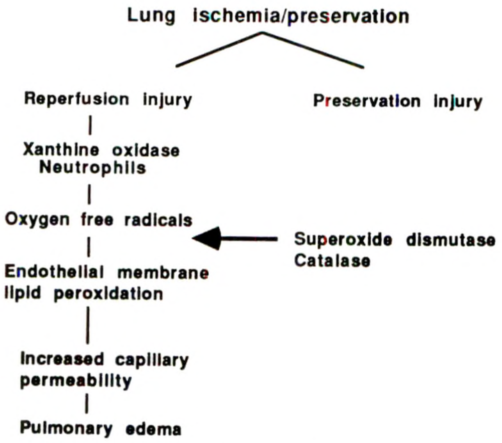

Fig 5. Hypothesis: reperfusion injury in the lung preserved for transplantation.

Finally, the present study did not correlate changes in extravascular lung water with changes in lung function such as partial pressure of arterial oxygen. In vivo studies from this laboratory involving warm lung ischemia and reperfusion have demonstrated higher partial pressures of arterial oxygen in OFRS–treated animals [20].

Despite these considerations, the current study suggests that the preserved lung undergoes a reperfusion injury mediated by oxygen free radicals. The injury is reduced by OFRS given at reflow. The use of OFRS may be a helpful adjunct to current hypothermic lung preservation.

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In Situ Prosthetic Graft Replacement for Mycotic Aneurysm of the Aorta

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Mycotic aneurysms as defined in this study include only those naturally occurring aortic aneurysms that result from or are secondarily infected by bacteria arising in a distant site of infection. Of the 2,585 patients treated for aortic aneurysm during the past 8½ years, 22 patients had disease conforming to this definition. The aneurysms were located in the ascending aorta in 2 patients, ascending aorta and arch in 5, arch and descending aorta in 1, descending thoracic aorta in 1, separate descending and abdominal aorta in 1, thoracoabdominal aorta in 5, upper abdominal aorta in 6, and infrarenal abdominal aorta in 1. The primary source of infection was the urinary tract in 2 patients, salmonellosis in 4, pneumonia in 3, subacute bacterial endocarditis in 2, ear, nose, and throat in 2, cellulitis of the hand in 1, chronic wounds in 2, dental extraction in 1, lumbar disc space infection in 1, septic thrombophlebitis in 1, and generalized febrile illness in 3. The duration of febrile illness ranged from 2 weeks to 1 year. All patients were treated with antibiotics and operation was performed within 24 hours after admission in 11 patients and within one to eight days after admission in 11. Treatment consisted of in situ graft replacement. Appropriate antibiotics were given intravenously for 4 to 6 weeks in patients with positive cultures and continued orally for the rest of the patients' lives. Of the 22 patients, 19 (86%) were early survivors, and all are still alive 3 months to 8 years postoperatively. Only 1 had a recurrent infection, which involved the intervertebral disc space.

(Ann Thorac Surg 1989;47:193–203)

The term mycotic was coined by Osler in the late 19th century for aneurysms that occurred in patients with subacute bacterial endocarditis [1]. The beaded gross appearance of the multiple aneurysms in these patients resembled a fungous growth, a finding that caused him to select the term *mycotic,* although he considered their pathogenesis to be destruction of arterial wall by embolization of infected material arising in the heart. The presence of such lesions indicated a "malignant" form of endocarditis because death was inevitable.

There has been a tendency in recent years to label all infected aneurysms as mycotic regardless of etiology. This report, however, is concerned only with naturally occurring aortic aneurysms that result from or are secondarily infected by bacteria arising in a distant site of infection. Thus, the aortic infections can be considered to be metastatic in origin. The pathogenesis of these aneurysms is embolization of infectious material into normal aortic wall, infection of defects in nonaneurysmal congenitally abnormal (coarctation of aorta and patent ductus arteriosus) or atherosclerotic aortic segments, or infection of intraluminal clot in preexisting atherosclerotic aneurysms by episodes of bacteremia. Infected aneurysms developing after aortic trauma or aortic operation (except inadequately treated mycotic aneurysms), contiguous infection (spine, urinary tract, pancreas, and aortic annulus abscess), and hollow viscus or airway aortic aneurysm erosion are excluded.

A review of the surgical literature regarding treatment of mycotic aortic aneurysms can be confusing. Thoracic surgeons generally recommend in situ graft replacement [2]. Peripheral vascular surgeons prefer excision, local debridement, and extraanatomical bypass [3–5]. The last form of treatment was not possible in most of the patients in this report because of the location of the aneurysm opposite the origin of a major vessel or in close proximity to the heart. In situ graft reconstruction with lifetime suppressive antibiotic therapy as previously described [6] was the therapeutic option, and the results of treatment in this setting should be of interest.

Material and Methods

Patients

During the 8½-year period from February 5, 1980, to August 21, 1988, aortic reconstruction was performed by the senior author (E.S.C.) for aneurysmal disease in 2,585 patients. Of these patients, 22 had an aneurysm that conformed to the definition of mycotic aneurysm already given, an incidence of 1 in 117 patients. There were 16 men and 6 women ranging in age from 42 to 75 years, with 18 being 60 years old or older and 9 being older than 70 years (Fig 1).

All 22 patients had a medically documented febrile illness that began 2 weeks to 1 year before the aneurysm operation by us (Fig 2). Nineteen patients had had one or

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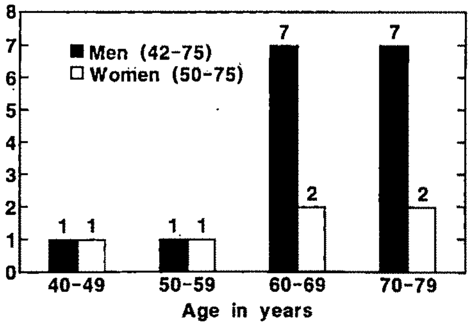

Fig 1. Age and sex incidence in 22 patients with mycotic aneurysm of the aorta.

Table 1. Primary Site of Infection

Site	No. of Patients	Deaths
Urinary tract infection	2	0
Salmonellosis	4	0
Pneumonia	3	0
Subacute bacterial endocarditis	2	0
Ear, nose, throat infection	2	0
Cellulitis of hand	1	1
Lumbar disc space infection	1	0
Chronic leg wound infection	1	0
Cervical laminectomy wound infection	1	0
Dental extraction	1	1
Intravenous line sepsis	1	1
Generalized febrile illness (no localization)	3	0
Total	22	3

more series of antibiotic treatments. Antibiotics were given for the primary infection or empirically in most instances. Three patients with recent onset had not had antibiotic therapy. Three other patients appeared "cured" of the infection after 6 weeks of intensive intravenous antibiotic treatment. Two of them had had subacute bacterial endocarditis, and the other had had *Staphylococcus aureus* septicemia secondary to pneumonia and bladder neck obstruction. Antibiotics had been discontinued for 2 months in the former 2 patients and the latter patient had just finished the second 6-week course of treatment. Nevertheless, 11 patients continued to be febrile at the time of admission, 6 had positive blood cultures, and 17 had positive cultures of the aneurysm contents.

The primary distant site of infection could be determined by appropriate culture or time sequence, or both, in 19 patients (Table 1). The offending organism was determined by blood culture (17 patients), by culture of aneurysm contents (17), or by both methods (19 patients) (Table 2). In 3 patients, cultures were not grown until antibiotics had been given for some time. The diagnosis of mycotic aneurysm was made in these patients based on a history of a major febrile episode and the location and nature of the aneurysmal process found at operation.

Numerous factors predisposing to infection were present. Those producing immunoincompetency are shown in Table 3 and others are shown in Table 4. The malignant lesions appeared to be controlled at the time of operation on the aneurysm and at follow-up. The gastrointestinal tract was thoroughly studied by endoscopy and contrast methods in the patient who had had *Streptococcus bovis* subacute bacterial endocarditis. The results of these examinations were normal, indicating that gastrointestinal disease including colon cancer was not a factor in this patient as has been reported in others [7].

The patient with aortic aneurysm infection caused by *Salmonella* sp and *Candida* sp was treated initially with antibiotics for 3 months. The infection recurred 2 to 3 months later and was again treated by antibiotics, removal of the infrarenal segment of the preexisting total abdominal aortic aneurysm, and an axillary–bilateral common femoral artery bypass graft. Cultures of the aneurysm contents grew *Salmonella* sp and *Candida* sp. The infection was treated with ampicillin and amphotericin B for 6 weeks. Infection recurred in the residual proximal aortic aneurysm 6 weeks after cessation of antibiotic therapy. Incomplete resection of aortic disease was the major factor in recurrence of the *Salmonella* sp infection,

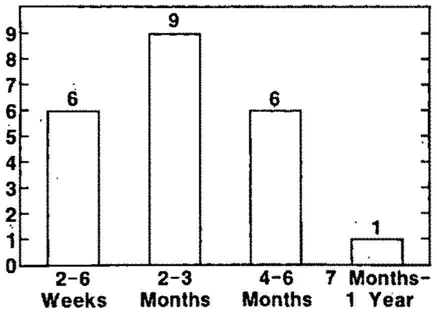

Fig 2. Interval between onset of febrile illness and aortic operation for mycotic aneurysm of aorta.

Table 2. Bacteriology

Bacteria	No. of Patients	Deaths
Staphylococcus aureus	5	1
Staphylococcus epidermidis	2	1
Salmonella sp	3	0
Salmonella sp + *Candida* sp	1	0
α-Hemolytic streptococci	2	0
Streptococcus bovis	1	0
Streptococcus pneumoniae	1	0
Haemophilus influenzae	1	0
Pneumococcus + *Haemophilus influenzae*	1	0
Escherichia coli	1	0
Edwardsiella tarda	1	0
No growth	3	1
Total	22	3

Table 3. Factors Predisposing to Immunoincompetency in 13 Patients

Factor	No. of Patients	Deaths
Steroids	6	0
Cytotoxic drugs	2	0
Alcoholism (severe)	2	0
Chronic renal failure (creatinine level, 3 mg/dL)	2	0
Irradiation	1	0

and multiple courses of antibiotic therapy undoubtedly were a factor in the fungous infection.

Aortic Pathology

An aneurysm was the principal aortic lesion found in these patients. It was sacciform in 18 patients and fusiform in 4. There were ten patterns of segmental involvement with multiple segments in three of these (Table 5). Sacciform aneurysms were frequently multiple and contiguous in origin ("stringed beads") within any single segment of the involved aorta (Fig 3). The aortic segment most frequently involved was that from which major arteries arose, the aortic arch in 6 patients and upper abdominal aorta in 12 (Figs 3–8). The sacciform aneurysms arose in the segment of aortic circumference opposite a vessel origin and involved the vessels in 4 patients (Figs 4, 5, 7, 8).

The walls of the sacciform aneurysms consisted of blood clot of varying age contained by compressed tissues in the mediastinum and retroperitoneum. Thus, they had ruptured at varying intervals and were false aneurysms. Recent rupture had occurred in 9 of the 18 patients with sacciform aneurysms, but none of the aneurysms had ruptured freely into a body cavity. Three patients had periaortic abscesses proximal and distal to the aneurysm, and all patients showed signs of inflammation around the aneurysm.

Table 4. Predisposing Factors in 19 Patients

Factor	No. of Patients	Deaths
Chronic idiopathic thrombocytopenic purpura treated with steroids and splenectomy	1	0
Chronic lymphocytic leukemia	1	0
Bladder cancer	1	0
Prostate cancer	2	0
Nephrotic syndrome	2	0
Chronic arthritis	4	0
Chronic obstructive pulmonary disease	10	0
Valvular heart disease	2	0
Diabetes	5	0
Dental extraction	1	1
Line sepsis after gastrectomy	1	1

Table 5. Location of Mycotic Aortic Aneurysm

Location	No. of Patients	Recent Rupture	Deaths (30-day)
Ascending aorta	2	1	0
Ascending aorta and arch	3	1	1
Ascending aorta, arch, descending aorta	1	1	0
Ascending aorta, arch, abdominal aorta with vessels	1	1	1
Arch and descending aorta	1	0	0
Descending aorta	1	1	1
Descending and abdominal aorta with vessels	1	1	0
Thoracoabdominal aorta with vessels	5	2	0
Abdominal aorta with vessels	6	3	0
Infrarenal abdominal aorta	1	1	0
Total	22	12	3

The sacciform aneurysms obviously arose about preexisting arteriosclerotic disease in 4 patients because skeletons of stony, hard material from the aortic wall were found traversing the aneurysms or were near the openings into the aneurysms. The openings into these aneurysms were usually irregular or ragged in contrast to the smooth, oval edges observed in patients with sacciform aneurysms of noninfectious origin. From studies performed before infection or during its early stages (plain roentgenograms, computed tomographic scans, and angiograms) showing uninvolved aortas, it is reasonable to assume that the aneurysms developed after the febrile illness started. A classic example is demonstrated in the following case report.

A 74-year-old man was seen with *Staphylococcus epidermidis* cellulitis on the dorsum of the hand secondary to trauma. This was treated with antibiotics, but abdominal pain, tenderness, and distention developed four days later. Plain chest and abdominal roentgenograms were normal (Fig 4A, top). An exploratory operation four days later resulted in negative findings. With continued antibiotics his condition improved, but chest roentgenograms made eight days after operation showed fracture of the preexisting calcified aortic wall of the upper descending thoracic aorta (Fig 4A, bottom), and a total aortogram revealed aneurysms of the transverse aortic arch and the abdominal aorta (Fig 4B). The former was replaced by a graft two days later. The abdominal aorta including the renal artery origins was replaced 13 days after the arch operation because of rupture of the enlarging abdominal aortic aneurysms (Figs 4B–D). *Staphylococcus epidermidis* was grown from cultures from both aneurysms. Aneurysmal disease of the aortic arch was documented to have developed within 15 days after onset of the hand infection.

The aneurysms were fusiform in 4 patients, and were

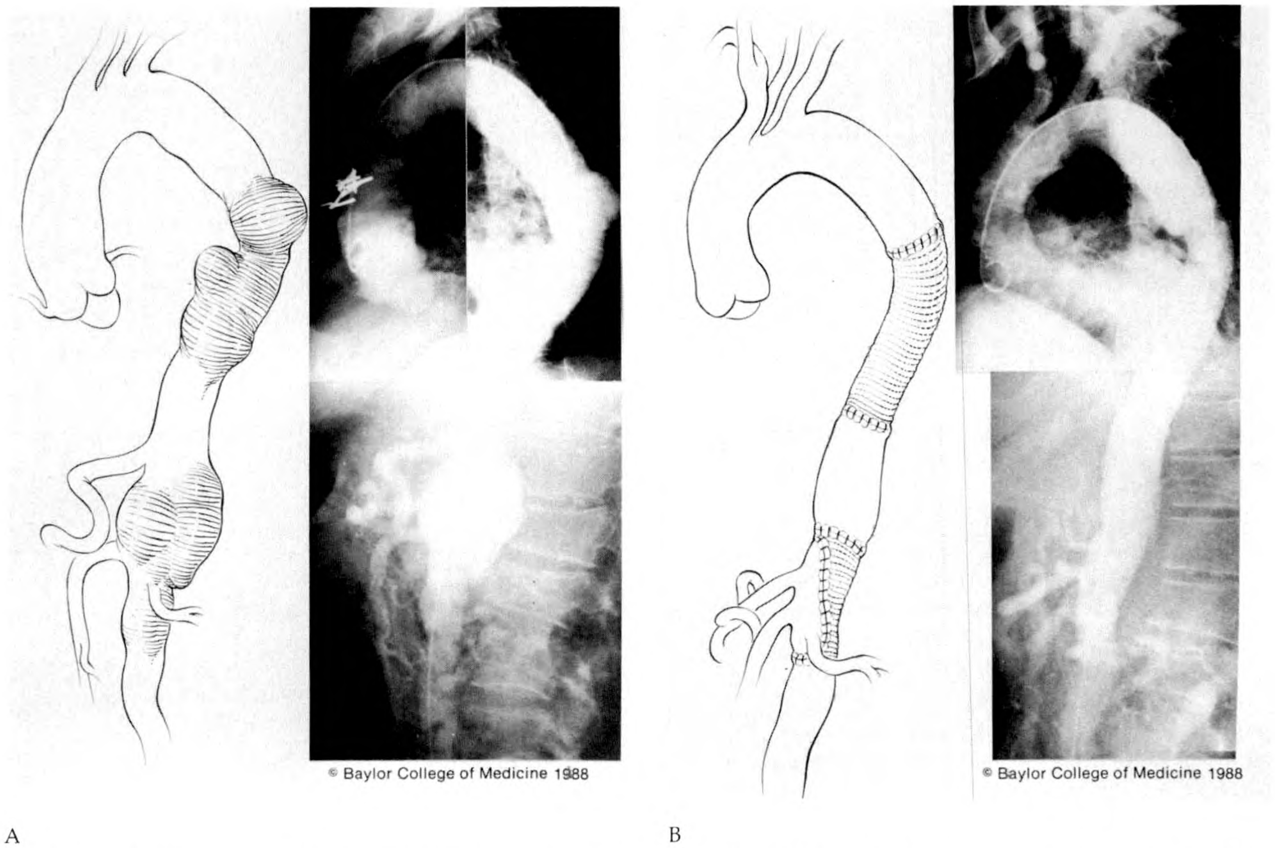

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Fig 3. Patient with multiple sacciform mycotic aortic aneurysms (Escherichia coli). *(A) Drawing and aortogram made before operation. (B) Drawing and aortogram made after operation.*

considered to be infected preexisting arteriosclerotic lesions. These aneurysms were noted either at operation or on computed tomographic scans before or at the beginning of infection. The aneurysm wall was intact at operation in 1 patient, and recent localized mural rupture had occurred in the other 3 patients. The aneurysm in 1 of the latter was located in the infrarenal abdominal aorta with bleeding into the abdominal cavity. Bleeding in the other 2 patients was contained in the retroperitoneal or mediastinal tissues. Nevertheless, rupture had occurred in a localized area, and the remaining aneurysm wall was intact.

Downstream mycotic aneurysms were present in distal branches of the hepatic and superior mesenteric arteries in 1 patient with primary aneurysmal involvement of the upper abdominal aorta just above the visceral vessels (Fig 8).

A previous operation had been performed in 5 patients with aneurysm. Three had undergone exploration. In 1 patient, excision of the left iliac artery and extraanatomical femorofemoral bypass were performed; another patient underwent excision of the infrarenal aortic segment of an aneurysm that involved the total abdominal aorta combined with an extraanatomical axillary–bilateral femoral artery bypass graft. A new mycotic aneurysm developed in the other iliac artery and the upper abdominal aorta in the former and in the residual proximal aortic segment in the latter after antibiotics were discontinued 6 weeks after operation performed elsewhere.

Clinical Manifestations of Aneurysm

The presence of an aortic aneurysm was known by the time of our hospital admission in all instances. Infection was suspected as the cause in 17, and other causes were suspected by the referring sources in 5 patients. Patients with aneurysms located in the descending thoracic and abdominal aorta had severe back pain, and some form of study (angiogram, computed tomographic scan, ultrasound, or plain roentgenograms) performed just before admission had demonstrated the presence of the aneurysms. Similar studies had shown the aneurysms in the ascending aorta and aortic arch. The aneurysmal symptoms in the latter included those related to superior vena caval obstruction, phrenic and recurrent laryngeal nerve paralysis, dysphagia, and airway compression. Other manifestations included fever, weight loss, anorexia, anemia, and leukocytosis. Most patients were in generally poor condition.

Treatment

Although the diagnosis of aneurysm had been established before admission in 22 patients, total aortography was performed by us in 21 because of the known frequency of multiple sites of aortic involvement. Moreover, this method of examination more clearly outlined the aortic branches and their relationship to the aneurysms. Computed tomographic scans were helpful in determining the presence of local rupture or surrounding inflammation.

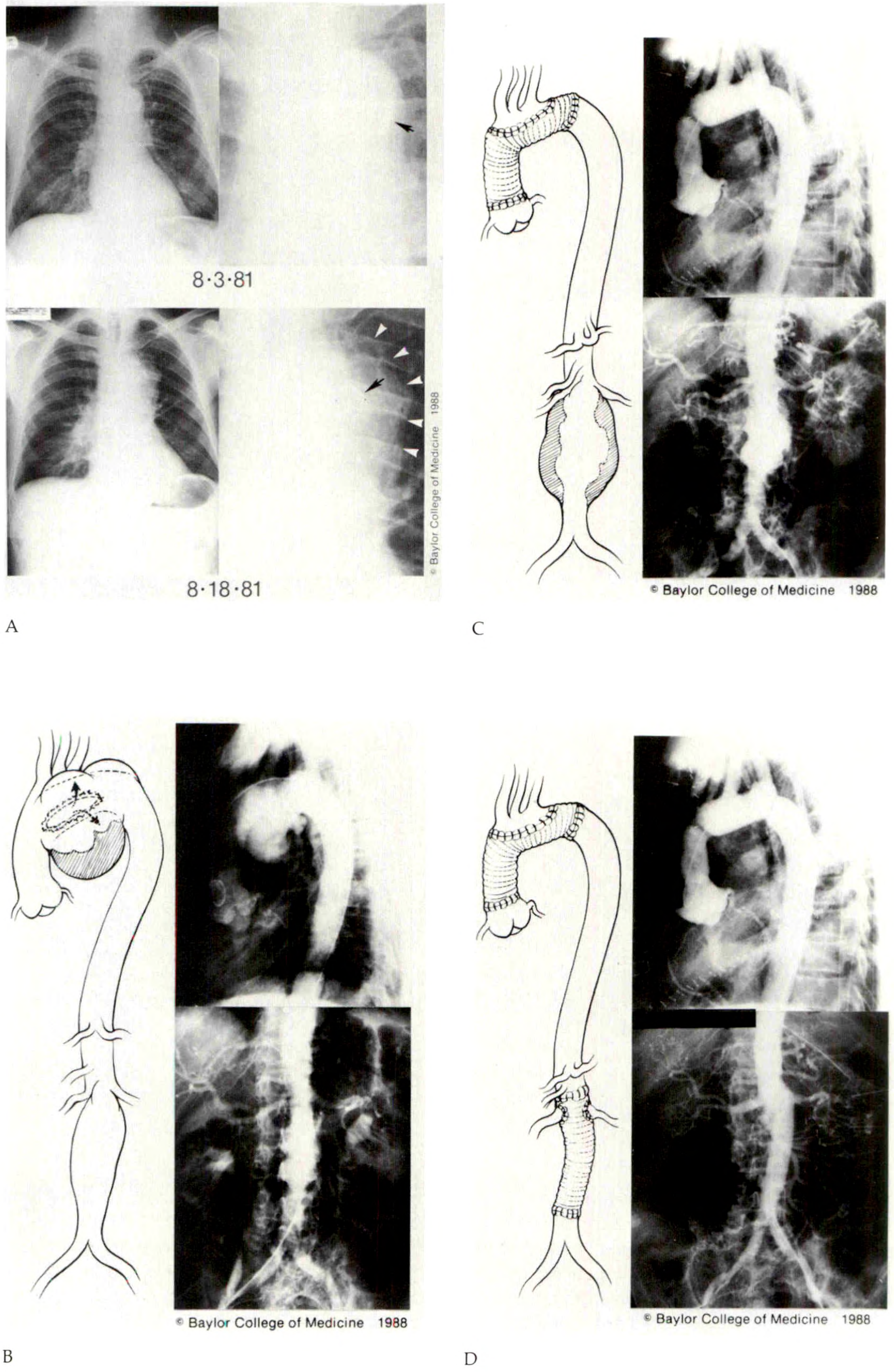
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Fig 4. Patient with multiple mycotic aneurysms (Staphylococcus epidermidis) *occurring after wound infection. (A) Plain chest roentgenograms made at the time of admission for abdominal pain (top) and again 15 days later (bottom). The latter roentgenogram shows fracture of calcification of aortic knob* (black arrows) *with surrounding soft tissue mass* (white arrowheads). *(B) Drawing and aortogram made before operation showing aneurysm of aortic arch* (arrows) *and abdominal aorta. (C) Drawing and aortogram made after arch replacement showing enlargement of abdominal aortic aneurysm. (D) Drawing and aortogram made after second operation showing grafts in place.*

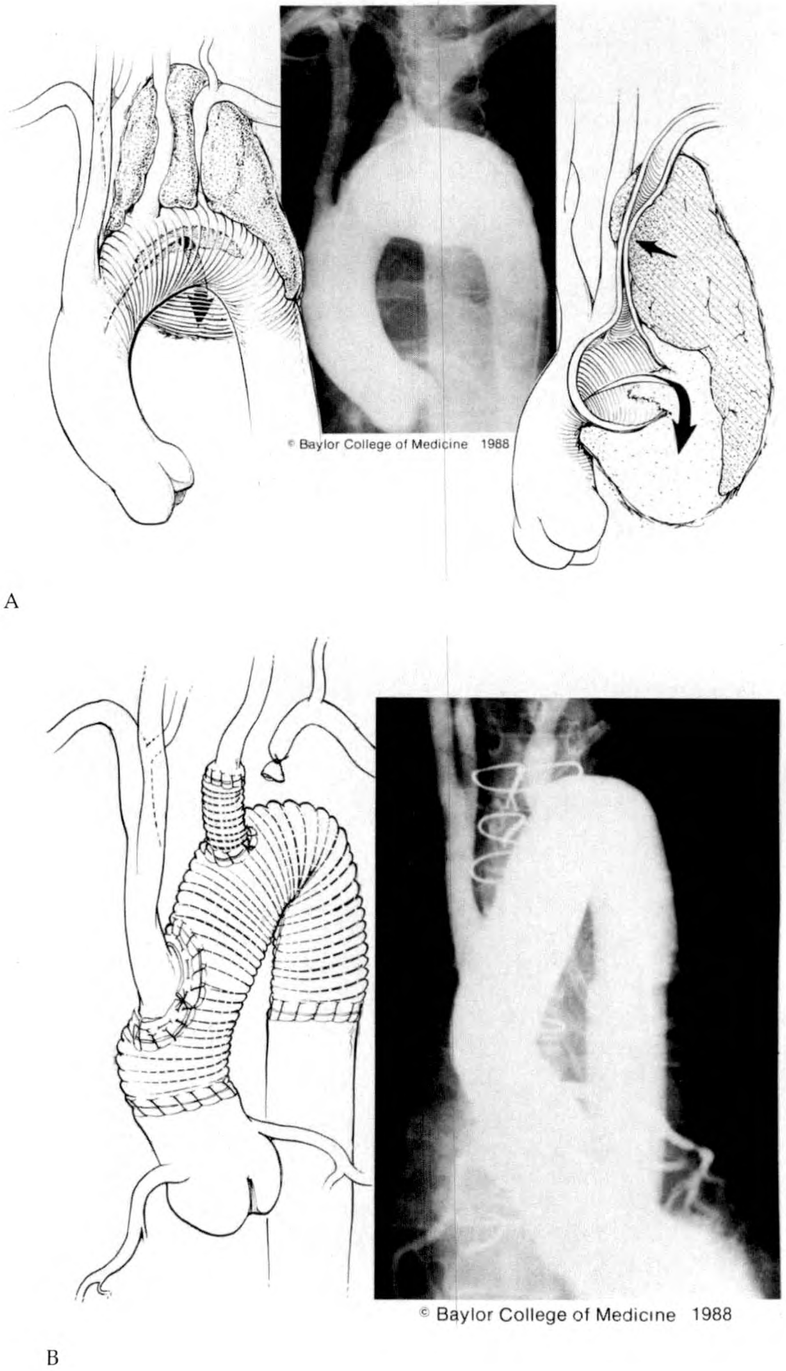
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Fig 5. Aneurysm (arrows) *of transverse aortic arch that developed during a long episode of sinusitis* (Streptococcus pneumoniae). *(A) Drawings and aortogram made before operation. (B) Drawings and aortogram made after operation.*

Thus, this method of study became routine in the more recently treated patients.

Early in the experience efforts were made to identify the involved bacteria, determine antibiotic sensitivity, and medically treat the patient until sepsis was controlled. Consequently, operation was delayed from one to eight days in 11 patients. However, rupture occurred in 2 of these patients, and signs of infection were rarely controlled. Moreover, the abdominal aneurysm remaining after graft replacement of the aortic arch in another patient ruptured 13 days after the arch replacement despite antibiotic therapy. As a result of this experience and the signs of rupture, operation was performed on the day of admission on 11 patients regardless of the state of infection.

All 22 patients were treated by placement of in situ Dacron grafts after evacuation of clot and local debridement using techniques previously described [6]. The 2 patients already referred to who had had a previous operation consisting of local excision of the left iliac artery and extraanatomical femorofemoral artery bypass in 1 and partial excision of a total abdominal aortic aneurysm (the infrarenal abdominal aortic section was removed) and axillary–bilateral femoral artery bypass graft had removal of the other iliac artery and the entire residual abdominal aorta in the former and removal of the residual upper

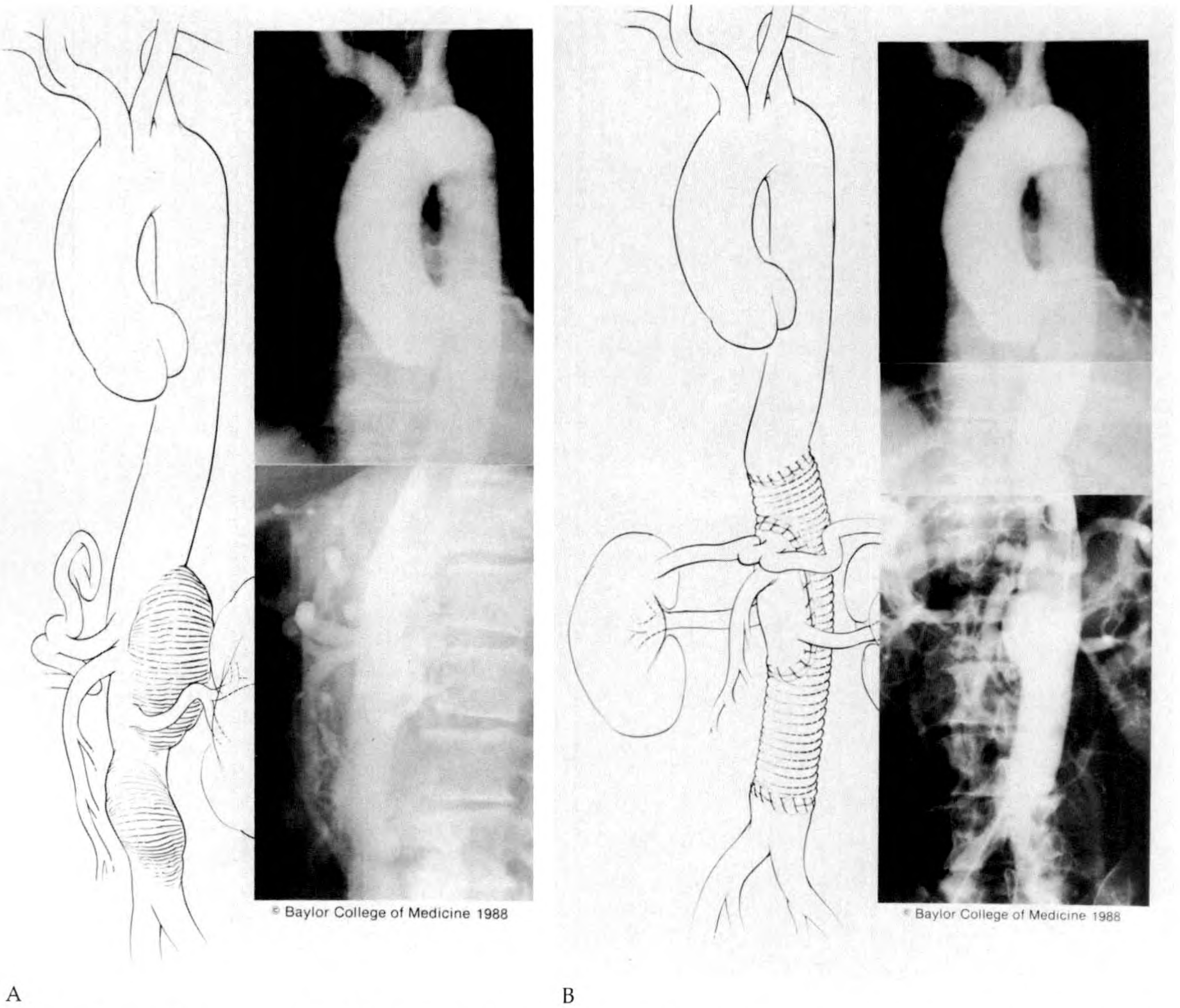
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Fig 6. Patient with mycotic aneurysm of the abdominal aorta from chronic Staphylococcus aureus *cervical laminectomy wound. (A) Drawing and aortogram made before operation showing location and extent of aneurysm. (B) Drawing and aortogram made after operation showing method of treatment.*

abdominal aorta in the latter. Visceral vessels were reattached to the graft, and peripheral circulation was maintained by the residual external iliac arterial system and the extraanatomical unilateral bypass in the former and by the extraanatomical bilateral bypass graft in the latter [6].

Patch graft angioplasty was employed in the treatment of 3 patients: 1 with a ruptured sterile aneurysm of the distal ascending aorta occurring from *S aureus* subacute bacterial endocarditis; 1 with a sterile aneurysm of the upper abdominal aorta due to *S aureus* after two courses of antibiotics, and 1 with a sterile aneurysm of the descending thoracic aorta. The distal aneurysm in the branch of the superior mesenteric artery was simply excised in the second patient to prevent later rupture (Fig 8). The other patient with controlled *S bovis* subacute bacterial endocarditis and a sterile aneurysm of the proximal tubular segment of ascending aorta had severe hemodynamic changes from aortic and mitral valve insufficiency. This patient was treated by double-valve replacement and separate graft replacement of the tubular segment of the ascending aorta. Of interest is the fact that the mitral valve was replaced through the aortic annulus as previously described [8].

The aneurysms in the remaining patients were replaced with tubular grafts. The patent brachiocephalic vessels in patients with aneurysms of the aortic arch were reattached directly to the graft in 5 patients and by separate tube graft in 1 patient using cardiopulmonary bypass, profound hypothermia, and circulatory arrest (Figs 4, 5) [6]. The visceral arteries were reattached directly to the grafts in 9 patients with involvement of the upper abdominal aorta. One or more of those vessels were reattached by separate Dacron grafts in 4 patients (Fig 7) [6].

Operation was performed in stages in 2 patients with separate aortic segmental involvement. The ascending aorta and transverse arch were involved in both and were replaced at the first operation. The separate descending thoracic aortic aneurysm in 1 patient was replaced at a separate admission 2 months later. The separate aneurysm involving the abdominal aorta in the other patient was replaced because of rupture 13 days after arch replacement, as already described.

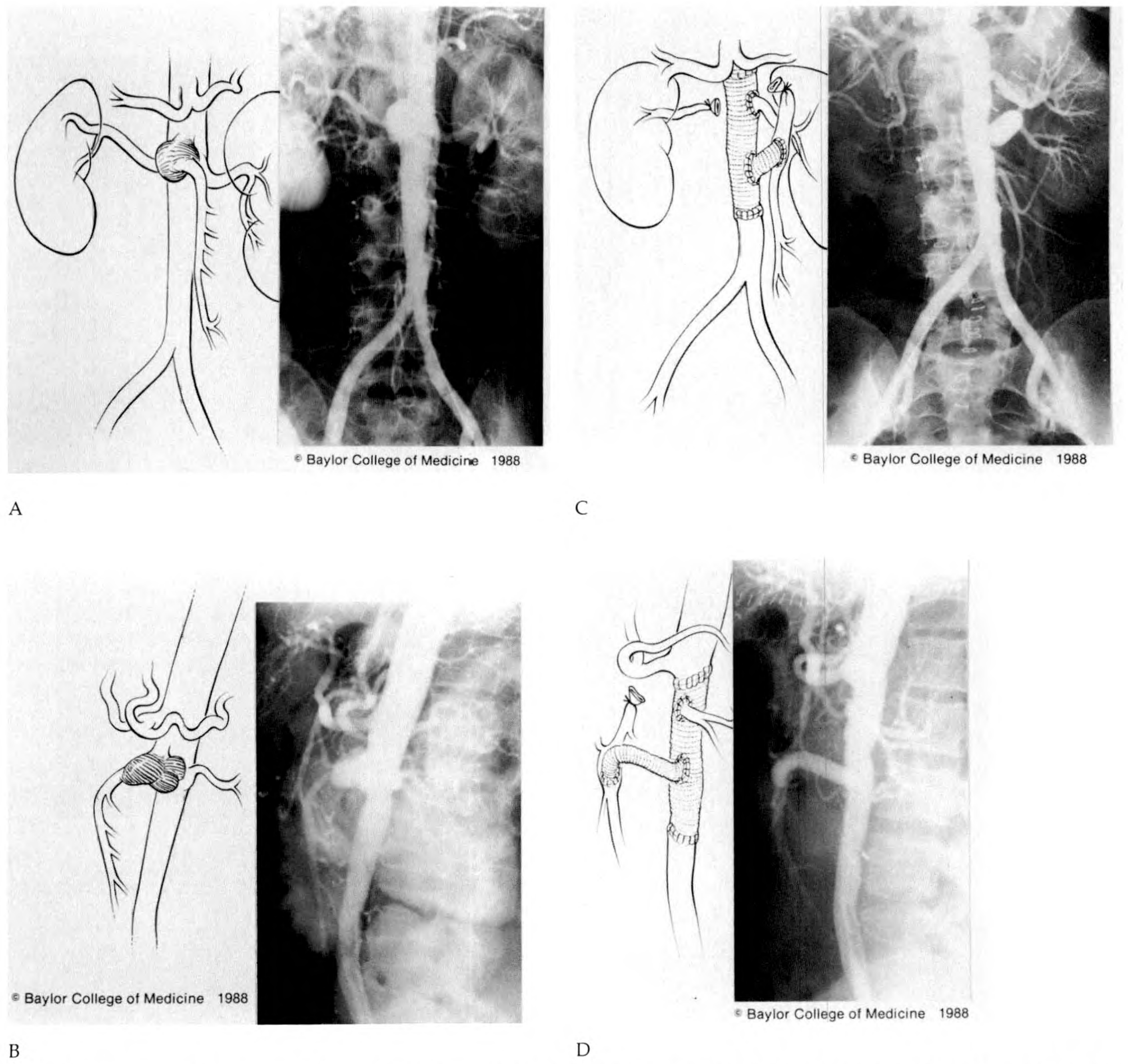

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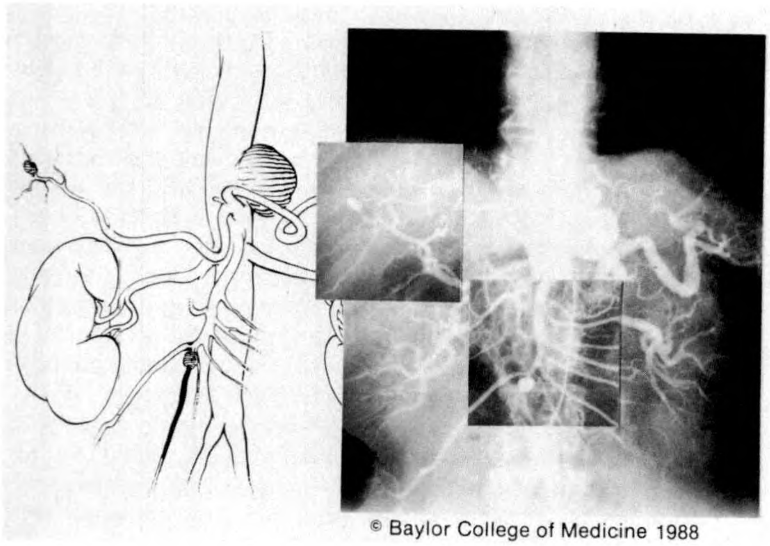
Fig 7. Patient with mycotic aneurysm (α-hemolytic streptococci) that developed during a period of chronic pneumonia. (A, B) Drawings and aortograms made in two projections before operation showing location and extent of involvement of vascular structures. (C, D) Drawings and aortograms made after operation showing method of reconstruction.

Appropriate antibiotic therapy was continued or started before operation when knowledge permitted. Otherwise, broad-spectrum antibiotics or our standard prophylactic antibiotic program was initiated. Antibiotic treatment was changed during operation when indicated by smears and Gram stains of operative specimens, or later as cultures and sensitivity studies indicated. The final antibiotic program was continued as an intravenous program for 4 (streptococci and gram-negative rods) to 6 weeks (staphylococci) and then was shifted to the oral route; this regimen was to be followed for the rest of the patient's life.

The 4 exceptions among surviving patients were 3 patients who appeared to have been cured of their infectious process before admission and 1 patient who had a drug allergy. Antibiotic therapy was discontinued 2 weeks to 3 months after operation in the former and at 3 years in the latter.

Results

Nineteen (86.4%) of the 22 patients treated were early (30-day) survivors and are still alive for periods ranging from 3 months to more than 7 years (Fig 9). Two patients were noncompliant regarding antibiotic treatment. One had thoracoabdominal aortic aneurysm replacement for an *S aureus* mycotic aneurysm in the region of the visceral vessels. This patient was doing well 13 days after operation, discharged himself against advice, and refused to take additional antibiotics. His family readmitted him five



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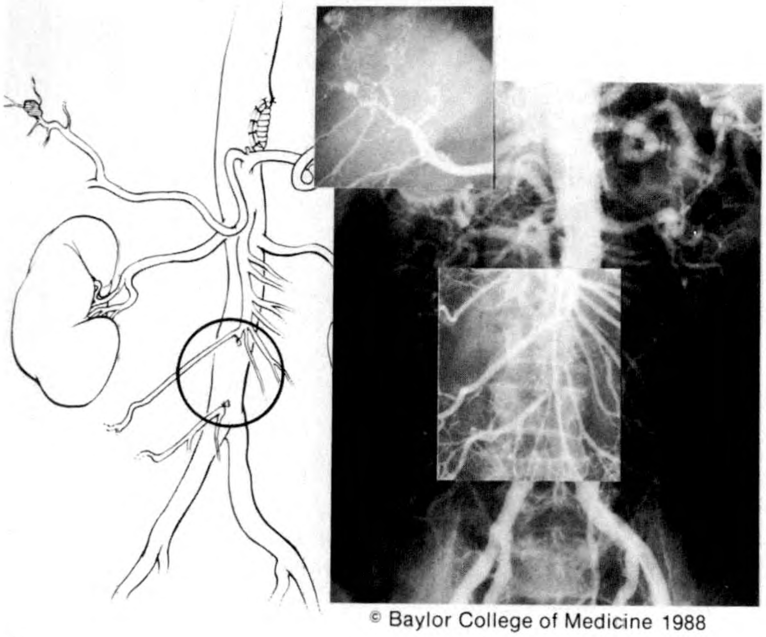

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*Fig 8. Patient with mycotic aneurysm (*Staphylococcus aureus*) that developed during the course of pneumonia associated with complications of bladder neck obstruction. (A) Drawing and aortogram made before operation showing sacciform aneurysm of aorta above visceral vessel origins and downstream aneurysm of hepatic and mesenteric artery branches. (B) Drawing and aortogram made after operation showing method of treatment.*

days later for chills and fever. He completed 6 weeks of intravenous therapy (vancomycin and nafcillin sodium) and was doing well at last follow-up (3 years, 30 days) on a regimen of 500 mg of cloxacillin orally four times a day. The other patient, a severe alcoholic who had graft replacement for a ruptured α-hemolytic streptococcal mycotic aneurysm of the infrarenal abdominal aortic aneurysm, discontinued antibiotic therapy soon after discharge and was readmitted 8 months later for an aortoduodenal fistula and α-hemolytic streptococcal aortic infection requiring reoperation. He was doing well at last follow-up 3 years, 5 months later on a regimen of chloramphenicol (500 mg) and amoxicillin (500 mg) orally four times a day.

The only patient with residual or recurrent infection at the time of follow-up was the patient already described who had multiple episodes of salmonellosis and was referred for recurrent infection in an incompletely removed abdominal aortic aneurysm. Initially, the patient did well after our complete replacement of the abdominal aorta, but then recurring *Proteus* sp urinary tract infection developed. Five months after operation, she now has a *Proteus* sp intervertebral disc space infection; however, the reconstructed aorta remains intact, and she continues to take cotrimoxazole daily to suppress the *Salmonella* infection. The *Proteus* infection is insensitive to antibiotics, and the patient refuses surgical drainage. The prognosis is poor.

The 3 deaths occurred in men 70 years of age or older. One was the 74-year-old man presented in the illustrative

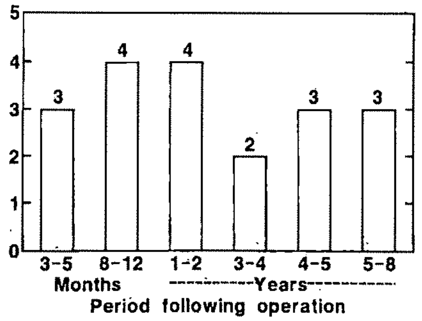

Fig 9. Length of follow-up for the 19 patients who survived operation.

case report who required emergency graft replacement of the abdominal aorta including renal artery origins for rupture 13 days after graft replacement of the ascending aorta and transverse aortic arch. Multiple complications occurred after the second operation, and the patient died 30 days after operation of multiple-organ failure. A 73-year-old man had uneventful graft replacement of the ascending aorta and transverse aortic arch. However, seven days after operation, he sustained a seizure, and aspiration associated with respiratory and cardiac arrest developed. The third patient was a 70-year-old man who had severe weight loss, renal failure requiring dialysis, and chronic obstructive pulmonary disease who died of multiple-organ failure seven days after graft replacement of the lower descending thoracic aorta.

Comment

The history or presence of febrile illness and local findings characteristic of acute or chronic infection in all aneurysms and positive blood and aneurysm cultures in most patients almost certainly confirm the diagnosis of mycotic aneurysm. Routine prospective cultures of abdominal aortic aneurysm contents obtained at operation have been reported to be positive in 15% of patients who did not appear to be infected, and their subsequent clinical course consisting of routine graft replacement and standard prophylactic antibiotic coverage in most instances was comparable with that observed in patients with negative cultures [9]. Thus, a positive culture from aneurysm content alone does not justify the diagnosis of mycotic aneurysm. This factor was considered in the diagnosis of these 22 patients.

Excision of the aneurysm was indicated because of expansion or rupture. These complications were not prevented in those patients in whom infection was controlled by antibiotics and occurred in 3 patients in whom operation was delayed for this purpose. Early operation, ie, within 24 hours of admission without regard to the status of the infection, evolved as a principle of therapy in these patients. This principle has been well established in the control of heart failure from valvular insufficiency due to subacute bacterial endocarditis [10–13]. Prosthetic valve replacement is frequently performed successfully for valvular insufficiency even in the presence of abscesses of the annulus and infected vegetation. The results of emergency graft replacement of a ruptured mycotic aneurysm of the descending thoracic aorta associated with coarctation in patients not treated with antibiotics were reported to be as good as those in treated patients [2].

The principle of in situ grafting before control of infection is well established, and such grafting is necessary in the majority of these patients. Extraanatomical bypass was impossible in 20 of the 22 patients because of the proximity of the heart or major aortic branches. The good results obtained by others in treating mycotic abdominal aortic aneurysm by in situ replacement suggests to us that the concept of extraanatomical bypass and local excision should be reassessed in view of the frequent complications associated with extraanatomical bypass [14, 15].

The required duration of antibiotic therapy is not well established. Adequately pretreated (4 to 6 weeks of intravenous therapy) patients who have had a satisfactory clinical response and are supported with antibiotic therapy during the operative period rarely need long-term antibiotic therapy except those with *Salmonella* sp infection. Although the latter can be adequately treated in this way, we believe that patients with this infection should be treated by suppressive antibiotic therapy for the remainder of their lives. Similarly, all patients with active infection, regardless of etiology, in whom an in situ graft is inserted should be given a full course of antibiotics intravenously (4 to 6 weeks) and then maintained on oral suppressive antibiotics for the remainder of their lives. This study does not provide the data to support this recommendation; however, our treatment of graft infection does. Moreover, one of us (T.W.W.) has data indicating that graft infections can recur up to 2 years after operation if suppressive antibiotics are stopped in such patients. Others [5] report similar recommendations.

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DISCUSSION

DR NICHOLAS T. KOUCHOUKOS (St. Louis, MO): In this excellent paper, Dr Chan and her colleagues have used a restrictive definition of mycotic aneurysm of the aorta by including only patients in whom the aneurysm resulted from or became secondarily infected by bacteria from a distant site. The infections were all considered to be metastatic.

Because of the high incidence of rupture, which occurred in 12 of the 22 patients, and the development of rupture in 3 of 12 patients who were receiving antibiotic therapy in an attempt to control the infection, the authors evolved a strategy of immediate operation after diagnosis, irrespective of the state of the infectious process or the duration of preoperative antibiotic therapy. Twenty of the 22 aneurysms involved segments of the aorta that contained major branches or were adjacent to the heart, and in situ grafting with Dacron was used in preference to extraanatomical bypass.

The principle of in situ grafting, embraced by thoracic surgeons for the treatment of infective endocarditis but generally resisted by vascular surgeons for the treatment of mycotic aneurysms of more peripheral arteries, appears to be an appropriate method of management for patients with the type of infections described in this report. With additional intravenous antibiotic therapy for 4 to 6 weeks for patients with active infection, and lifetime oral antibiotic therapy for all patients, which appears to be an essential and critical component of the treatment regimen, excellent long-term survival and freedom from infection have been achieved. One cannot argue with success.

I have two questions for Dr Chan. Only bacterial infections were included in this series. Can this treatment strategy be applied to aneurysms infected by other agents such as fungal organisms? Also, can it be applied to mycotic aneurysms that occur in association with infected vascular prostheses, trauma, or infections of contiguous tissues or organs?

DR F. E. E. VERMEULEN (Nieuwegein, the Netherlands): I'd like to join the other discussant, Dr Kouchoukos, in congratulating Dr Crawford's group for a fine presentation and excellent results.

We reviewed our own experience at the Antonius Hospital in Nieuwegein and found some discrepancies. However, at the time of the analysis we included patients with a less restrictive definition, including those with aortopulmonary fistulas.

Between 1971 and 1987 we operated on 507 patients with thoracic aneurysms of the thoracic or thoracoabdominal aorta. One hundred three patients had descending aortic aneurysms, and in this subgroup we found five of our eight mycotic aneurysms.

It is specifically in this subgroup and in the arch localization that the concept of in situ grafting can be challenged. Indeed, in the ascending aorta and the thoracoabdominal aorta an extraanatomical derivation is somewhat unrealistic.

We approached 3 patients with an ascending aorta to abdominal aorta derivation and exclusion of part of the descending thoracic aorta. One patient had an aortopulmonary fistula. All 3 survived, 2 for 10 and 8 years; the third died of a cerebral cancer 4 years later.

We used in situ replacement in 5 patients, including 2 with thoracoabdominal localizations. Two of the 5 had recurrent rupture after the repair of the descending thoracic aorta, after 4 weeks and 6 months, respectively, and both died.

I would like to ask Dr Chan to comment on our opinion that we should at least reconsider bypass and exclusion whenever this is possible, as in the mycotic aneurysms of the descending thoracic aorta.

DR CHAN: We thank the discussants for their comments and the additional knowledge that they have presented regarding the subject of mycotic aneurysms of bacterial origin. We have had very little experience in the treatment of fungal infection of the aorta and cannot answer the question regarding the best form of treatment. In treatment of postoperative graft infections of the ascending aorta and transverse aortic arch, we have had the best results using suture closure of infected false aneurysms and graft wrap with muscle flaps or omentum combined with the antibiotic protocol outlined in the paper. Replacement of infected composite valve grafts is performed only when valve function is impaired or in cases with emboli. Distal graft infection may be treated either by excision and extraanatomical bypass or in situ operation with suppressive antibiotics. In other cases, successful results have been obtained by percutaneous tube drainage and irrigation with antibiotic solution and lifetime suppressive antibiotic therapy. We would prefer the latter two methods.

Pneumothorax in Cystic Fibrosis: A 26-Year Experience

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We reviewed the records of all patients with cystic fibrosis and radiologically demonstrated pneumothorax at Rainbow Babies and Childrens Hospital between 1959 and 1987. There occurred 144 pneumothoraces, 71 right and 73 left, in 99 patients, 48 female and 51 male. The median survival from the date of the first pneumothorax was 29.9 months. Primary therapy included the following: observation; tube thoracostomy; tube thoracostomy with instillation of quinacrine hydrochloride, tetracycline, silver nitrate, or talc; or partial pleurectomy. Complications were minimal in each group. The surgical group did significantly better than all other groups except the group given talc. We conclude that pneumothorax is a late and ominous complication of cystic fibrosis. The primary treatment of pneumothorax should be partial pleurectomy. Talc instillation should be reserved for patients in respiratory failure who are too ill to undergo operation and for the occasional patient in whom surgical intervention fails.

(Ann Thorac Surg 1989;47:204–7)

The incidence of pneumothorax in patients with cystic fibrosis has increased as improved treatment has resulted in prolonged survival [1]. This complication tends to occur in older patients with severe pulmonary disease [2, 3]. Ideal treatment of the pneumothorax would be quick, safe, and effective, and would result in permanent prevention of recurrence. Treatment has varied from simple observation to open thoracotomy with pleurectomy and abrasion [4–6]. We present our results, which include some very long (ie, > 10 year) follow-ups. The data suggest that although pneumothorax is a late and ominous complication of cystic fibrosis, partial pleurectomy is a safe and very effective treatment.

Material and Methods

Cystic fibrosis was diagnosed by a positive sweat test and either typical pulmonary or digestive symptoms or a positive family history. All patients with cystic fibrosis who were seen from 1959 to 1987 and who had any radiological evidence of extrapulmonary pleural air were included. Only patients whose pneumothoraces were treated at our center were included.

Recurrence was defined as a pneumothorax that occurred after complete radiological resolution of a pneumothorax for at least 1 week after removal of the last chest tube. Treatment failure was defined as persistent substantial pneumothorax or continuing air leak for more than 2 weeks after therapy.

All information was obtained by chart review. Clinical scoring was performed by our modification [7] of the method of Shwachman and Kulczcyki (S-K score) [8]. Statistical analysis included the use of life tables, the χ^2 test, and the Fisher exact test.

Many patients in all treatment groups received supplemental oxygen in low to moderate concentrations (ie, an inspired oxygen fraction < 50%). All patients received high doses of antibiotics intravenously beginning no later than the day of admission; some patients already were on a regimen of intravenous administration of antibiotics when the pneumothorax occurred. Other routine therapy for cystic fibrosis was continued and included segmental postural drainage (as tolerated), aerosolized bronchodilators and antibiotics, pancreatic replacement, and supplemental vitamins.

Chest tubes were inserted under local anesthesia and, occasionally, sedation with an intravenously administered narcotic. Chemical pleurodesis was accomplished by infusing the sclerosing agent (quinacrine hydrochloride, 100 mg; tetracycline, 500 to 1,000 mg; or talc, 10 g) into the pleural space through the chest tube. The patient was then rotated in various positions to expose the entire surface of the pleura to the sclerosing agent. This procedure was performed once a day for three days when quinacrine or tetracycline was used and generally once for talc. Silver nitrate pleurodesis was done in the operating room under general anesthesia.

Pleurectomy was performed through an axillary or anterolateral muscle–splitting incision. In the upper thorax, the visible parietal pleura was removed; the remainder of the pleural surfaces were abraded. Any active air leak or large blebs were oversewn or stapled. In 1 patient with a bilateral pneumothorax, the surgical approach was through a median sternotomy, which allowed access to both pleural cavities.

Results

Of 1,268 patients with cystic fibrosis who were followed between 1959 and 1987, 99 had at least one episode of

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Table 1. Pneumothoraces Treated During Each Period

Years	No. of Pneumothoraces
1960–1965	3
1965–1970	15
1970–1975	21
1975–1980	36
1980–1985	49
1985–1987	20

pneumothorax. Forty-eight patients were female and 51 were male. Thirty-nine patients had eventual involvement on both sides; 1 patient was initially seen with bilateral pneumothoraces. There were 144 episodes (71 right and 73 left) of pneumothorax in these 99 patients. The incidence has been increasing over the years (Table 1).

The average age at diagnosis of cystic fibrosis was 2.75 years, and the average age at diagnosis of pneumothorax was 19 years (range, 7 to 35 years; median age, 17 years). Table 2 shows the age distribution in each sex. More male patients were seen at an older age, probably because of their longer survival. The median survival from the date of the first pneumothorax was 29.9 months (range, 0 to 206 months) (Fig 1).

Seven primary treatment approaches were used over the study period. They included the following: observation alone; chest tube alone; chest tube with quinacrine, tetracycline, silver nitrate, or talc pleurodesis; or pleurectomy and abrasion (Table 3).

Observation

Observation alone was used in 28 patients (average S-K score, 54). As a group, these patients were in stable condition and only minimally compromised by a small pneumothorax. Only 14 patients (50%) experienced primary resolution, and a pneumothorax recurred in 4 patients.

Thoracostomy Alone

A varying number of chest tubes (range, 1 to 4) were used as the only treatment in 39 patients (average S-K score, 43). Only 12 (31%) experienced uncomplicated primary resolution; 2 of them had recurrence. Two patients sustained substantial hemorrhage from chest tube insertion, and 1 of them needed a thoracotomy for control of the hemorrhage and repair of the lung laceration. The average hospital stay was 22 days.

Table 2. Age and Sex Distribution of Patients With Cystic Fibrosis and Pneumothorax

Age (yr)	Male	Female
<10	3	7
10–20	39	41
20–30	30	17
30–40	5	2

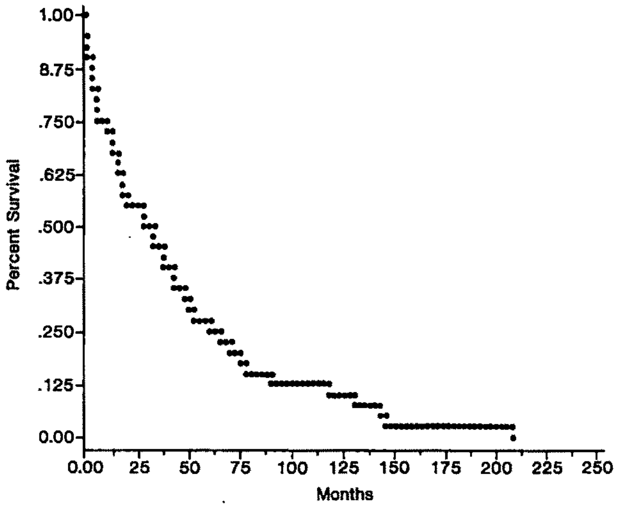

Fig 1. Percent survival plotted against time from first pneumothorax. Median survival was 29.9 months.

Quinacrine Pleurodesis

Nine patients (average S-K score, 53) were treated with quinacrine pleurodesis. Five experienced uncomplicated resolution with no recurrence. Average length of hospitalization was 15 days. In 4 patients resolution did not occur, and surgical intervention was necessary.

Talc Pleurodesis

Five patients were treated with talc as the primary therapy. All had resolution of pneumothorax, but 1 patient died ten days after the instillation of talc.

Tetracycline Pleurodesis

Two of the 4 patients treated with tetracycline pleurodesis had resolution; 1 of them had recurrence. In the other 2 patients resolution was not accomplished, and surgical intervention was necessary.

Silver Nitrate Pleurodesis

The 2 patients treated with silver nitrate pleurodesis did not have resolution and needed further therapy. Silver

Table 3. Initial Therapy

Therapy	No. of Patients	No. of Resolutions	No. of Recurrences
Observation	28	14	4
Thoracostomy	39	12	2
Pleurodesis			
Quinacrine	9	5	0
Tetracycline	4	2	1
Silver nitrate	2	0	. . .
Talc	5	5	0
Pleurectomy and abrasion	57	54	6

Pleurectomy and abrasion was significantly better ($p < 0.01$) than observation, thoracostomy, quinacrine, tetracycline, and silver nitrate.

nitrate was used early in our experience and has not been used in 20 years.

Pleurectomy and Abrasion

Of 57 patients (average S-K score, 53) who underwent surgical intervention, failure to obtain primary resolution occurred in 3. One patient had a continued left-sided air leak after bilateral pleural abrasions performed through a median sternotomy. There were six recurrences (11%) among the remaining 54 patients. One patient died on day 7 of a tension pneumothorax on the nonoperative side. In 1 patient, phrenic nerve paralysis caused considerable difficulty; nerve function improved within 4 weeks, but the patient died of respiratory failure on the 52nd postoperative day. There were no wound complications.

Comment

Pneumothorax is an ominous complication of cystic fibrosis. Median survival after the first pneumothorax was 29.9 months. A contralateral pneumothorax eventually occurred in 40% of our patients. Subsequent survival was usually short.

One explanation for the grim survival figures for this complication is that patients with cystic fibrosis who experience a pneumothorax generally have very advanced pulmonary disease [1], which has a correspondingly poor prognosis, and would not have survived long anyway. However, it seems reasonable to hypothesize that the pneumothorax itself and related treatment contributed to the poor survival. Morbidity associated with unresolved leaks can be devastating. Pneumothorax and its treatment cause restrictive pulmonary disease, which, no doubt, contributes substantially to the subsequent downhill course. Schuster and colleagues [6] reported that pulmonary function did not change significantly after pleurectomy or pleurodesis. We attempted to look at pulmonary function before and after treatment, but because of the extreme variability over time and in each patient group, no valid statistical analysis could be performed.

A very high recurrence rate has been described after observation or tube thoracostomy only [9]. We had 29% and 17% recurrence rates, respectively. Pleurectomy and abrasion, quinacrine pleurodesis, and talc pleurodesis have been reported to have low recurrence rates [1, 4–6]. Quinacrine pleurodesis did result in a very low recurrence rate; however, only 5 (56%) of 9 patients achieved initial resolution.

In our hands, partial pleurectomy has been the most effective treatment for pneumothorax in patients with cystic fibrosis. There is a low complication rate and a 95% success rate. It is significantly better ($p < 0.01$) in achieving primary resolution than observation, thoracostomy alone, or chemical pleurodesis with quinacrine, tetracycline, or silver nitrate. Even patients with severely compromised pulmonary function came through the operation and the postoperative period amazingly well. The vast majority of patients (90%) were extubated in the operating room or within five hours postoperatively. By using a small axillary or anterolateral muscle–splitting incision, postoperative pain was kept to a minimum, and analgesic control with maintenance of cough, particularly after the first postoperative day, was possible. Unlike other series [10, 11] in which major complications such as bleeding or extrapulmonary infection occurred in up to 10% of the patients, we have not experienced any such problems. An additional advantage of surgical intervention is that in a substantial number of patients, the site of the air leak can be found and oversewn. Also, the chest tubes can be accurately placed under direct vision.

Talc poudrage has been very effective, although we have had only a small experience with it to date. At present, *United States Pharmacopeia*-certified pure talc is free from contamination with asbestos, a known carcinogen [1]. Concern about asbestos contamination lessened the use of talc in the past. Talc poudrage does have the advantage of not requiring anesthesia or a surgical incision, although the patients still have considerable discomfort after treatment. Patients with active air leaks have the risks of talc aspiration and pneumonitis. Adhesions from talc also appear to be very dense and virtually eliminate the possibility of future operation in the event of hemoptysis, abscess, or bronchopleural fistula.

Our data indicate that partial pleurectomy is the best primary therapy for pneumothorax in patients with cystic fibrosis. Patients in severe respiratory failure who are unable to undergo an operation and patients who refuse an operation should be offered closed thoracostomy tube placement and talc poudrage.

This study was supported in part by grant DK 27651 from the National Institutes of Health and grants from the Cystic Fibrosis Foundation and the United Way Services of Greater Cleveland.

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DISCUSSION

DR BLAIR KEAGY (Chapel Hill, NC): The authors have elegantly discussed a problem that will assume greater clinical importance as the life expectancy of cystic fibrosis victims increases. In their manuscript, however, they do not elaborate on the pathophysiology of the pneumothorax. In lung biopsy specimens from patients with cystic fibrosis, Braman noted hypertropy of the bronchial glands, mucus plugs, and fibrosis, whereas Tomashefski described distorted elastic fibers, vascular proliferation, columnar vacuolated mesothelial cells—the so-called Dunhill lesions—and air cysts. I would appreciate the authors' comments regarding the gross and microscopic findings from their operative specimens.

Therapeutic decisions are based on the initial failure rate and the frequency of late ipsilateral recurrence. Using data from Table 3, we can examine the percentage of late recurrences only in those patients who resolved with initial therapy. The rate of recurrence after pleurectomy and abrasion was 9%, that of tube thoracostomy was 17%, and that of the chemical pleurodeses grouped together was 8%. There is no statistical difference among these groups. Would the authors therefore agree that an attempt should first be made to resolve the problem nonoperatively?

Data from the paper do certainly show a higher initial failure rate with most of the nonoperative modes of therapy. An exception is the talc pleurodesis, with which complete resolution was achieved in all 5 patients in whom the procedure was attempted. This was confirmed in another study reported by Tribble and co-workers from the University of Virginia, who followed 5 patients, aged 9 to 22 years, for up to 4 years after talc pleurodesis without evidence of recurrence.

In the present study the authors state that disadvantages of talc pleurodesis include the possibility of talc aspiration and the formation of dense adhesions that prevent future thoracotomy in the event of hemoptysis, abscess, or bronchopleural fistula. To better compare the risks of pleurectomy versus the use of talc, I would appreciate having the authors inform us how often these late operations actually do occur.

In this study, some of the partial pleurectomies and pleurodeses were carried out using an axillary approach. We found this incision to be quite successful in patients with congenital apical blebs. However, it is difficult to excise blebs in other areas of the lung using this approach. Do the authors note the pathology in their series to be primarily in the lung apex?

Recent reports such as one in the August 1987 issue of the *British Medical Journal* describe heart-lung transplantations in individuals with end-stage cystic fibrosis. If this trend continues in the future, do the authors feel that the scarring that results from either chemical or surgical sclerosis of the pleural cavity will prevent or make more hazardous later organ transplantation?

And, finally, with regard to the initial 69% failure rate with tube thoracostomy, did the lung fail to expand due to insterstitial fibrosis or pleural scarring, or was there a persistent air leak from a diseased bronchus? Also, why did 2 of 39 patients have significant hemorrhage during chest tube insertion? Are there vascular adhesions in the pleural space that make thoracostomy tube insertion more hazardous in patients with cystic fibrosis?

DR SPECTOR: Dr Tomashefski, at Rainbow Babies and Childrens Hospital, did autopsies on the majority of these patients and described the findings and pathophysiology in his paper. Certainly we've seen a changing patient profile with cystic fibrosis. Most of the patients are now treated with steroids and are of a much older age group. We do not feel that nonoperative therapy should be tried first because the period that patients have a chest tube in place or are being treated with another modality is time lost from being out of the hospital and able to undergo adequate postural drainage and other therapy. Therefore, we feel that the best therapy should be the first one.

We've also noted that the patients whose original therapy failed and who went on to have second therapy of either quinacrine, tetracycline, talc, or operation, had a good resolution rate and fairly low recurrence rate. However, surgical treatment, when performed after a previous therapy, had a slightly higher incidence of complications. One patient had a wound infection. One can postulate that this patient had a chest tube in for a long period of time and was previously treated with Atabrine, which may have increased the chance of wound infection. There were also 2 patients who had substantial bleeding postoperatively, and this may be due to increased adhesion formation after the initial treatment.

The surgical approach, a high axillary incision, gives very good exposure to the apex, in which the majority of the blebs are found. The other place that blebs are found is in the superior segment of the lower lobe, which is also easily accessible through this incision.

The question of lung transplantation is something that we have thought about, although it's not really our therapy that's eliminating patients from the possibility of receiving a transplant. It is the fact that they have a pneumothorax that has to be treated that's eliminating them from transplantation.

Patients with cystic fibrosis have very stiff lungs and often have adhesions. Therefore, chest tube placement is not without its risks, and the lung and adhesions can be torn.

Cryopreservation of Canine Trachea: Functional and Histological Changes

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Section of General Thoracic Surgery, Division of Thoracic Diseases and Internal Medicine, and Division of Pathology, Mayo Clinic and Mayo Foundation, Rochester, Minnesota

The purpose of this study was to evaluate tracheal viability and to document histological changes in an autograft implanted in the abdominal wall after a 1-week period of cryopreservation. A 5-cm segment of cervical trachea was resected in 6 dogs. One-half of the segment was cryopreserved and stored in liquid nitrogen at −196°C for 1 week. The other half was immediately implanted in an abdominal pouch fashioned from the rectus abdominis muscle (control). One week later, the cryopreserved segment was thawed and then implanted in a similar contralateral muscular pouch. Five weeks later, the control and cryopreserved autografts were removed and compared with the in situ trachea. Ciliary beat frequency was assessed by transmitted light technique. Histology was evaluated by light microscopy. Gross anatomy and mucus production were maintained after cryopreservation. Histologically the cryopreserved segment displayed both normal epithelium and smooth muscle cells, but the cartilage was abnormal as characterized by empty lacunae. Mean ciliary beat frequency of in situ, control, and cryopreserved segments was 13.3 ± 1.8, 13.5 ± 1.5, and 13.3 ± 1.1 beats per second (± the standard deviation), respectively. We conclude that smooth muscle, epithelium with mucus production, and ciliary function were retained after cryopreservation and reimplantation. Histological changes, however, were suggestive of early cartilage ischemia. These findings support further evaluation of cryopreserved canine tracheal grafts.

(Ann Thorac Surg 1989;47:208–12)

Indications for a tracheal prosthesis are currently limited to those patients in whom the length of the diseased tracheal segment precludes primary repair [1]. Because an ideal prosthetic substitute does not exist [2], efforts to reconstruct large tracheal defects with homograft trachea seem logical. Results with the cryopreserved vascular homograft [3, 4] have prompted us to evaluate cryopreserved trachea as a potential solution to this problem. The purpose of this study was to document functional and histological changes after implantation of a cryopreserved tracheal autograft in an animal model.

Material and Methods

Experimental Design

Six adult mongrel dogs weighing 27.0 ± 4.3 kg were used, and each served as its own control. Anesthesia was induced with intravenous administration of sodium pentobarbital (30 mg/kg). Under aseptic conditions and spontaneous ventilation without an endotracheal tube, a cervical tracheal segment 5 cm in length was resected, and continuity was reestablished with interrupted 4-0 Prolene sutures.

The excised trachea was divided in half, and one of the 2.5-cm segments (control) was buried immediately in an abdominal wall muscle pocket fashioned from the rectus abdominis muscle. Within 30 minutes after harvesting, the remaining 2.5 cm of trachea was cryopreserved. The freezing medium was Dulbecco's modified Eagle's medium (Gibco, Grand Island Biological Company, New York, NY) with a final concentration of 20% fetal calf serum and 10% dimethyl sulfoxide. A plastic sterile bag containing the specimen was filled with the freezing medium, sealed, and frozen in a computer-controlled unit at approximately 1°C per minute to −90°C. The bag was then stored in liquid nitrogen (−196°C) for 1 week.

After a week, the specimen was thawed by placing the bag in a 37°C ethanol bath for five minutes and then rinsing the segment with fresh Dulbecco's modified Eagle's medium. At a second operation in the same animal, the cryopreserved trachea was immediately implanted in a similar contralateral abdominal wall muscular pocket.

All animals were killed 5 weeks after the first operation using intravenously administered 26% sodium pentobarbital (0.3 mL/kg). The control and cryopreserved tracheal segments were dissected from their respective muscular pockets. A portion of the native trachea was also harvested. Gross appearance, mucus production, and tracheal diameter were recorded for each of the three specimens (Fig 1).

Throughout the experiment, animal care complied with the "Principles of Laboratory Animal Care" and the "Guide for the Care and Use of Laboratory Animals."

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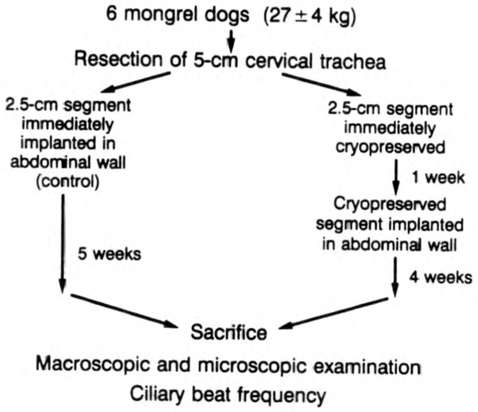
6 mongrel dogs (27 ± 4 kg)
Resection of 5-cm cervical trachea
2.5-cm segment immediately implanted in abdominal wall (control)
2.5-cm segment immediately cryopreserved
1 week
Cryopreserved segment implanted in abdominal wall
5 weeks
4 weeks
Sacrifice
Macroscopic and microscopic examination
Ciliary beat frequency

Fig 1. Experimental design used to document functional and histological changes after cryopreservation and reimplantation of canine trachea.

This study was approved by our institutional animal care committee.

Histology and Ciliary Beat Frequency Determination

A representative ring from each specimen was fixed in 10% buffered formalin, embedded in paraffin, and stained with hematoxylin and eosin for histological studies. A second representative ring was prepared for determination of ciliary beat frequency [5]. Rings were freed of mucus, divided into thirds, and incubated in Roswell Park Memorial Institute 1640 tissue culture medium, 1.5% bovine serum albumin, and 0.2% glutamine for one to two hours at 37°C to stabilize ciliary activity. A small fragment of ciliated mucosa from each third of the tracheal ring was placed on a 0.5-mm welled glass slide and covered with a coverslip. The preparation was viewed at ×400 using phase contrast with a Zeiss microscope.

A special eyepiece with a fiberoptic probe 450 μm in diameter (EG & G Gamma Scientific, San Diego, CA) was used to isolate a small area containing approximately 40 to 100 cilia. As the cilia beat across the eyepiece, the intensity of light changed. The light was then directed through the fiberoptic probe to a photomultiplier, where the variations in light intensity were amplified by a photometer (laboratory photometer model 110; Pacific Instruments, Concord, CA), and the electric signal was printed on an electrocardiographic strip-chart recorder [6]. A 2-second paper strip was recorded for each sample, and the ciliary beat frequency was determined. The ciliary beat frequency re-

Table 1. Macroscopic Characteristics of Tracheal Rings

Ring	Mucous Plug	Incorporation	Diameter[a,b] (cm)
In situ	0	0	2.1 ± 0.2
Control	6	6	2.1 ± 0.4
Cryopreserved	6	6	2.3 ± 0.2

[a] Data are shown as the mean ± the standard deviation. [b] Significance: $p > 0.05$.

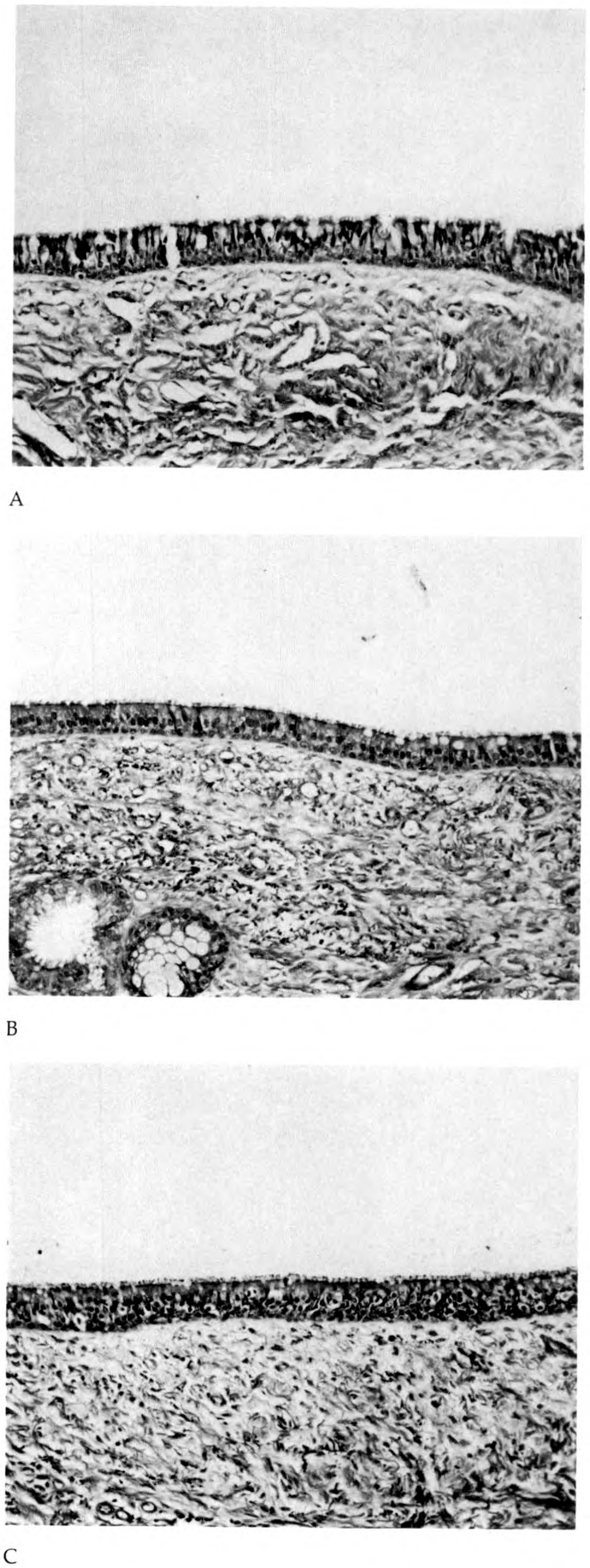

Fig 2. Histological sections of trachea demonstrating epithelium in (A) in situ, (B) control, and (C) cryopreserved specimens. (H & E; ×250 before 68% reduction.)

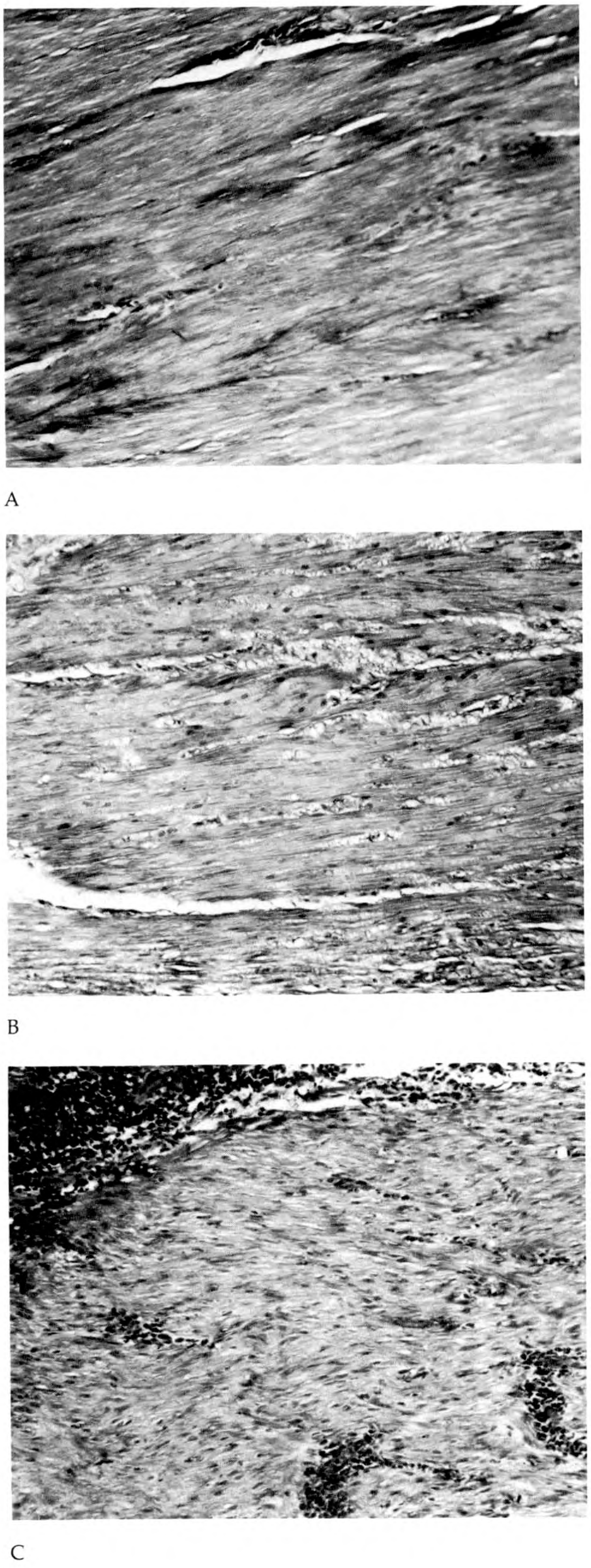

Fig 3. Histological sections of trachea demonstrating smooth muscle in (A) in situ, (B) control, and (C) cryopreserved specimens. (H & E; ×250 before 68% reduction.)

ported for each ring was the mean of the frequencies determined from the three separate segments.

Student's t test for paired observations was used as the measure of statistical significance.

Results

All 6 dogs survived the staged surgical procedures to harvest and reimplant the control and cryopreserved tracheal segments without complications. At the time of death, all wounds were well healed, and the animals were active and eating well.

Macroscopic characteristics are summarized in Table 1. The control and cryopreserved segments were macroscopically well incorporated into the muscular pocket by surrounding tissue. All implanted specimens appeared grossly normal and exhibited a central mucous plug. Ring diameter of the in situ, control, and cryopreserved segments was 2.1 ± 0.2, 2.1 ± 0.4, and 2.3 ± 0.2 cm (± the standard deviation), respectively ($p > 0.05$).

Histologically, the cross section of the tracheal wall in both the control and cryopreserved segments displayed normal structural integrity when compared with the native trachea. The epithelium in all three specimens demonstrated pseudostratified columnar features with well-identified ciliated, mucous, and basal cells (Fig 2). The smooth muscle in the membranous portion of the trachea was grossly and histologically viable (Fig 3). The tracheal hyaline cartilages in all segments maintained their horseshoe shape, and there was no disruption of cartilaginous architecture. The results of microscopic examination of the in situ and control cartilages were normal. Examination of the cryopreserved cartilage segments, however, showed loss of chondrocyte nuclei in the lacunae without inflammation. This finding was interpreted as ischemia with loss of chondrocytes (Fig 4).

Mucus production and active synchronically beating cilia were present in all specimens. Mean ciliary beat frequency of the in situ, control, and cryopreserved segments was 13.3 ± 1.8, 13.5 ± 1.5, and 13.3 ± 1.1 beats per second, respectively ($p > 0.05$) (Fig 5).

Comment

Devascularization of the trachea produces major structural changes that successfully preclude their use as "free" grafts [7–9]. Attempts to prevent these changes have led to varying results. Experimentally, tracheal autografts wrapped with omentum healed with stenosis, usually secondary to chondromalacia in the midportion but with well-preserved cartilage at both suture lines [10]. In a similar trial, bronchial autografts wrapped with intercostal muscle resulted in normal mucosa, viable bronchial cartilage, and a well-healed suture line [11]. In our study, muscle was selected as the tissue to revascularize the control and cryopreserved specimens because of the better success with intercostal muscle to provide blood supply to an ischemic bronchus [11].

Because cryopreservation has been successful with other types of homografts [3, 4], the application of this technique to tracheal replacement seemed logical. To

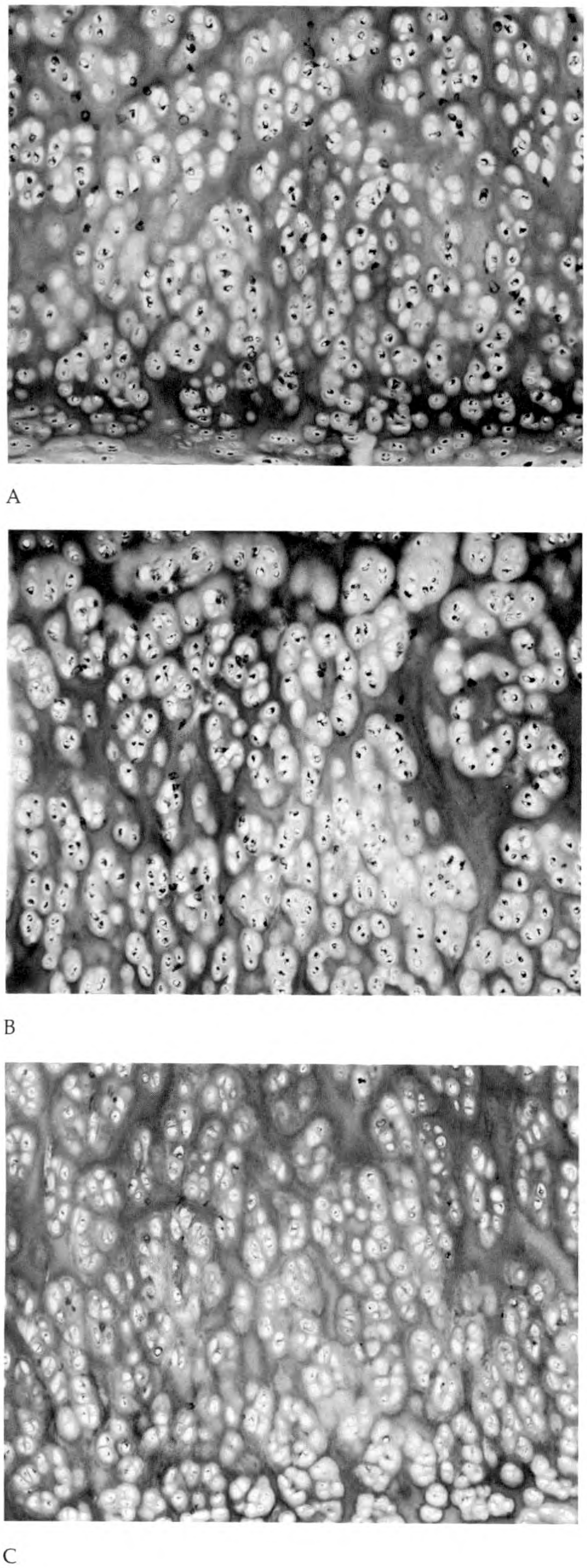

Fig 4. Histological sections of trachea demonstrating hyaline cartilage in (A) in situ, (B) control, and (C) cryopreserved specimens. (H & E; ×160 before 68% reduction.)

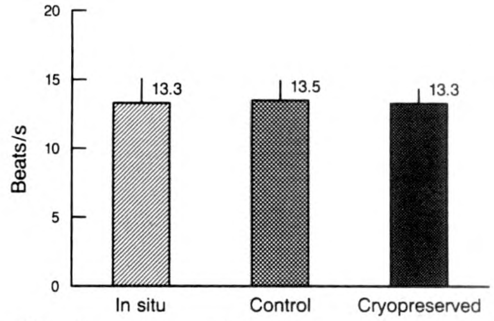

Fig 5. Ciliary beat frequency of the in situ, control, and cryopreserved tracheal segments. Values are shown as the mean ± the standard deviation (p > 0.05).

document changes after cryopreservation, we modified a model used to study carcinogenesis in subcutaneously implanted tracheal heterografts [12, 13] and bronchial autografts [14, 15]. In our study, the cilia, epithelium, and smooth muscle survived cryopreservation well. Our findings support previous reports of normal histological architecture after application of a cryoprobe to either the external [16] or the mucosal [17] surface of the canine trachea. That this may also apply to humans is suggested by the finding of ciliary motility in cryopreserved human nasal mucosal biopsy specimens [18].

Hyaline cartilage was most affected histologically. Most likely this was secondary to ischemia, although inadequate diffusion of the cryoprotectant may be another possible cause [19]. Ischemia, however, seems more likely, as similar histological findings in cartilage have been reported after pressure injury from a tracheostomy cuffed tube [20].

The feasibility of this technique to provide a tracheal substitute needs further evaluation. The short time-frame of this experiment does not allow a conclusion on the ultimate fate of the cartilage, and additional studies are necessary to better define the long-term fate of the cartilage after cryopreservation [21]. Also, the technique used to revascularize a transplanted tracheal conduit in the clinical setting, whether it is with muscle or omentum, needs to be further developed [10, 11, 22]. Finally, the antigenicity [23] of tracheal transplants is not completely known. If these issues can be resolved successfully, it may be possible in the future to have a replacement trachea available for patients who need it.

We conclude that cryopreservation and subsequent muscle revascularization of the canine trachea maintains gross anatomy, ciliary function, and mucus production. Histological changes are suggestive of early cartilage ischemia despite intact epithelium and smooth muscle.

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Long-term Results in Neonates With Pulmonary Atresia and Intact Ventricular Septum

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Our entire institutional experience with pulmonary atresia and intact ventricular septum (1965 through 1987) included 115 patients, 16 of whom died before surgical intervention. Fifty-six percent of surgical patients (n = 99) had angiographic evidence of right ventricle–coronary arterial connections. The early mortality in the surgical group was 27.2%, and the actuarial survival was 24.7% ± 6% at 13 years postoperatively. Multivariate analysis indicated that the presence of ventriculocoronary connections ($p = 0.037$), a decreasing ratio between right ventricular and left ventricular pressure at the initial cardiac catheterization ($p = 0.007$), and lower weight at operation ($p = 0.001$) were incremental risk factors for postoperative death; the presence of Ebstein's anomaly was an additional risk factor in the overall experience (including patients not surgically treated) ($p = 0.01$). Nearly all long-term survivors underwent at least one reoperation, including right ventricular outflow tract reconstruction (n = 39) and thromboexclusion of the right ventricle (n = 9). The presence of severe stenosis or interruption of the proximal left anterior descending coronary artery system was a uniformly lethal risk factor for patients undergoing these procedures ($p = 0.0003$). We conclude that surgical procedures that successfully decompress the right ventricle will usually result in biventricular circulation in and long-term survival of patients with pulmonary atresia with intact ventricular septum not complicated by Ebstein's anomaly or extensive ventriculocoronary connections. Decompression or thromboexclusion of the right ventricle is contraindicated in patients with ventriculocoronary connections and a right ventricle–dependent coronary circulation.

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Information concerning the overall results with the complete spectrum of palliative and definitive surgical procedures in patients with pulmonary atresia and intact ventricular septum is limited, and the long-term results for a large cohort of such patients are unknown. Moreover, there is limited information concerning the surgical results in patients with pulmonary atresia and intact ventricular septum complicated by the presence of ventriculocoronary (VC) connections, who in contemporary experience constitute an important group of patients with this anomaly.

Material and Methods

A 22-year institutional experience (January 1965 to October 1987, The Hospital for Sick Children, Toronto) with pulmonary atresia and intact ventricular septum included 115 patients. Sixteen of these 115 patients died in the neonatal period before surgical intervention, and the analysis of the surgical experience pertains to the remaining 99 patients. All patients were determined from a detailed review of the angiographic and surgical records to have an atretic pulmonary valve, a perforate tricuspid valve, an intact ventricular septum, and concordant atrioventricular and ventriculoarterial connections; specifically excluded were patients with associated tricuspid atresia, functional pulmonary atresia, and critical pulmonary stenosis.

Ventriculocoronary Connections

Ventriculocoronary connections were present in 50 (56%) of the 89 patients in whom this determination could be reliably made from the angiographic records. A detailed retrospective review of the angiograms was made for all patients undergoing transannular patch reconstruction of the right ventricular outflow tract (RVOT) (n = 39) and a subset of 9 patients undergoing thromboexclusion of the right ventricle. Based on right ventricular and aortic injections and without knowledge of the clinical outcome, patients were categorized in terms of (1) the presence and specific location of VC connections and (2) the presence or absence of a major (greater than 50%) reduction in the luminal diameter of the proximal or middle segments of the left anterior descending coronary artery (LAD) system. This information was then used in a separate multivariate analysis of risk factors for patch reconstruction of the RVOT.

Associated Cardiac Lesions

Among the 99 surgical patients, important associated cardiac lesions exclusive of coronary artery malformations were unusual. There were 4 patients with congenital aortic stenosis. Four patients had Ebstein's anomaly of the

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Table 1. Initial Operation for Pulmonary Atresia and Intact Ventricular Septum

			30-Day Mortality	
Procedure	No. of Patients	Early Deaths	%	70% Confidence Limits
Shunt only	48	8	16.7	11.0%–24.1%
Pulmonary valvotomy + shunt	33	11	33.3	24.1%–43.8%
RVOT patch	12	5	41.7	24.6%–60.5%
Pulmonary valvotomy only	5	2	40	10.3%–71.0%
Aortic valvotomy	1	1	100	

RVOT = right ventricular outflow tract.

tricuspid valve, and 2 additional patients had a grossly enlarged right ventricle that was without the tricuspid valve anomalies characteristic of Ebstein's malformation and that could be considered variants of Uhl's anomaly [1]. Unroofed coronary sinus syndrome, endocardial fibroelastosis, and partial anomalous pulmonary venous drainage occurred in 1 patient each. Three patients had both the right and left coronary arterial systems connected to the aorta by a single ostium.

Follow-up

Follow-up was accomplished by review of clinical records, cardiac catheterization and angiographic data, and surgical, autopsy, and outpatient records or by telephone interview with physicians or families if the final follow-up dates were not in either 1986 or 1987 (n = 6). Thus, the cases of 100% of the patients were reviewed from 1986 onward. The mean follow-up for survivors of the initial operation was 7.9 years and the maximum length of follow-up was 21.6 years.

Data Analysis

The Statistical Analysis System LIFE TEST procedure was used to generate specific Kaplan-Meier product-limit survival curves [2]. The Cox proportional hazards linear regression model was used to isolate risk factors for death occurring any time postoperatively [3], with the Breslow modification [4] invoked for tied data. The backward elimination option was utilized in the PHGLM procedure in the Statistical Analysis System with a p value of 0.10 or less necessary for inclusion in the model. The independent variables considered in the analysis included the following: sex, VC connections (yes/no), right ventricular to left ventricular pressure ratio, weight at the first operation, pulmonary valvotomy at the initial procedure (yes/no), and use of prostaglandin therapy.

Results

Almost all patients had surgical intervention within the first 2 weeks of life. Most patients underwent a systemic–pulmonary shunt with or without concomitant pulmonary valvotomy (Table 1). Pulmonary valvotomy was most commonly performed using the transarterial approach. In the entire experience, a Potts shunt was used most frequently; however, over the past decade, the modified Blalock-Taussig interposition shunt has been used almost exclusively.

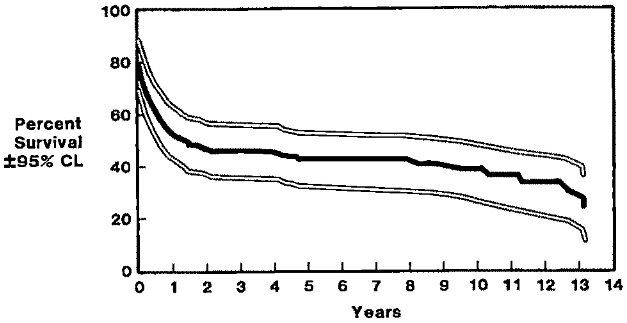

Fig 1. Patient survival after initial operation for pulmonary atresia with intact ventricular septum. White bars enclose 95% confidence limits (CL).

Experience with RVOT reconstruction at the primary operation was limited to 12 patients. Three patients successfully underwent simple transannular RVOT patch repair; 3 of 4 patients having open RVOT repair in conjunction with other intracardiac procedures including atrial septal defect closure died. Right ventricular outflow tract reconstruction using a closed technique [5] was unsuccessful in 3 of 5 patients: 2 required early reoperation, and 1 died intraoperatively.

Survival Analysis

The overall survival (± the standard error of the mean) of the surgical patients (n = 99) was 24% ± 6% at 13 years postoperatively (Fig 1). The results of multivariate analysis of incremental risk factors for early and late postoperative death are indicated in Table 2. The association of the lower right ventricular to left ventricular pressure ratio at the initial cardiac catheterization with reduced postoperative survival is largely attributable to the 9 deaths among the 11 patients with a ratio less than 1.0. Most of these patients had grossly enlarged right ventricles with or without Ebstein's malformation of the tricuspid valve. There was a smoothly continuous increased survival among infants with a greater body weight at the time of the initial operation. A separate analysis of the total experience (n = 116), which included the 16 patients who

Table 2. Incremental Risk Factors for Initial Surgical Intervention[a]

Variable	p Value	β
Ventriculocoronary connections	0.037	0.61
Right ventricular to left ventricular pressure ratio	0.007	−0.99
Weight	0.001	−0.77

[a] The Cox stepwise proportional hazards general linear model procedure was used; p (model) = 0.0003.

Table 3. Right Ventricular Outflow Tract Reconstruction in 39 Patients with Pulmonary Atresia and Intact Ventricular Septum

			Mortality	
Repair	No. of Patients	Early Deaths	%	70% Confidence Limits
RVOT (total)	39	16	41.0	33.0%–48.7%
With PVR or conduit	8	3	37.5	16.2%–61.6%

PVR = pulmonary valve replacement; RVOT = right ventricular outflow tract.

died before surgical intervention, identified the presence of Ebstein's anomaly as an additional risk factor (p = 0.01).

Late Operation

Nearly all long-term survivors underwent at least one reoperation. Reconstruction of the RVOT was performed in 39 patients (Table 3). The mean age at the time of this procedure was 2.0 years, and this includes 12 patients undergoing this procedure in the neonatal period. Reconstruction of the RVOT was performed in conjunction with orthotopic pulmonary valve replacement in 7 patients, and 1 patient underwent interposition of a valved conduit between the right ventricle and the pulmonary artery. Seven patients had partial or complete closure of an atrial septal defect performed simultaneously.

Ventriculocoronary Connections

Ventriculocoronary connections were present in 15 (40.5%) of 37 patients in whom this determination could be made from the coronary cineangiograms; in all but 2 patients, these fistulas connected both to the LAD and to the right coronary artery. Noteworthy was the finding that there were no operative survivors after RVOT reconstruction among patients with VC connections complicated by stenosis (n = 5) or interruption (n = 2) of the proximal LAD. Two patients with obstructive lesions involving the distal segment of the LAD were long-term survivors. By multivariate analysis, the presence of obstructive lesions within the proximal LAD system was highly significantly associated with decreased survival after RVOT reconstruction (p = 0.0003). The actuarial survival after RVOT reconstruction was 38.7% ± 9.9% at about 9 years postoperatively (Fig 2).

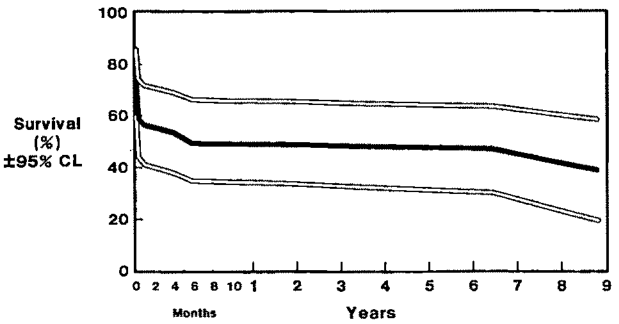

Fig 2. Patient survival after right ventricular outflow tract reconstruction. White bars enclose 95% confidence limits (CL).

Thromboexclusion of Right Ventricle

A subset of 9 patients with tiny right ventricles, absent infundibular component, and conspicuous VC connections underwent thromboexclusion of the right ventricle after the method described by Waldman and colleagues [6]. This procedure included patch closure of the tricuspid valve and atrial septectomy (n = 9), insertion of thrombogenic coils into the right ventricle (n = 5), and a central shunt (n = 6). The presence of severe stenosis or interruption of the LAD without distal collaterals was a unifying feature in all 4 operative deaths, and was absent in the 5 surviving patients.

Other Reoperations

Other types of reoperation, not mutually exclusive, included the following: repeat pulmonary valvotomy with (n = 6) or without (n = 2) an associated Glenn procedure; a Glenn shunt (n = 8) either as an isolated procedure (n = 1) or in conjunction with atrial septal defect closure (n = 3), pulmonary valvotomy (n = 2), closure of a Blalock-Taussig shunt (n = 1), or thromboexclusion of the right ventricle (n = 1); closure of an atrial septal defect performed alone (n = 1) or in association with a Glenn procedure (n = 1) or pulmonary valve replacement (n = 1); and a modified Fontan procedure (n = 3, 2 of whom had previously undergone thromboexclusion of the right ventricle). All patients whose reoperation included pulmonary valvotomy, a Glenn procedure, atrial septal defect closure, or a modified Fontan procedure survived.

Comment

This study unequivocally demonstrates the surgical importance of VC connections and associated obstructive lesions in the coronary arteries of patients with pulmonary atresia and intact ventricular septum. Our experience with an inclusive spectrum of surgical approaches involving a large cohort of patients confirms the relatively high risk attending various surgical procedures designed to decompress the obstructed right ventricle. Multivariate analysis of our overall experience indicated that the risk of death at any time was incrementally increased in infants with a low birth weight and when the morphological findings included Ebstein's anomaly of the tricuspid valve or coronary artery anomalies in the form of VC connections. In the surgical group, the risk of death was relatively high for the first 2 postoperative years (48% actuarial survival at 2 years) and then was succeeded by a phase of more modest mortality risk extending beyond 12 years from the time of the initial surgical procedure (Fig 1).

The presence of VC connections has long been recognized in pulmonary atresia with intact ventricular septum, as has the predilection for the development of fibrous intimal hyperplasia resulting in obstructive lesions in the native coronary circulation [1, 7, 8]. The notion that surgical decompression of the right ventricle may lead to myocardial infarction in the presence of high-grade lesions in the proximal coronary arterial system was previously advanced by Freedom and colleagues [1], and the surgical significance of this finding was illustrated by O'Connor and associates [9] in a single case report. The so-called right ventricle–dependent coronary circulation is especially precarious in a setting of hypertensive and grossly hypertrophied ventricular mass, and the susceptibility to myocardial ischemia can be further aggravated by reduced diastolic pressures consequent to systemic–pulmonary shunts and the presence of systemic hypoxia.

Our experience indicates that VC connections occur in more than one half of infants with pulmonary atresia and intact ventricular septum and that the fistulous communications usually involve both the left and right branches of the coronary circulation. A histopathological study of 23 cardiac specimens of pulmonary atresia and intact ventricular septum from our institution [10], all from babies less than 1 week of age, demonstrated a high incidence of coronary arterial involvement, especially with severe right ventricular hypoplasia. Most of these patients had old replacement fibrosis of the myocardium in association with extensive coronary arterial dysplasia, findings suggesting prenatal onset of this disease process.

Our retrospective review of the coronary cineangiograms in the subset of patients undergoing RVOT repair ($n = 39$) and thromboexclusion of the right ventricle ($n = 9$) indicates that VC connections are usually complicated by high-grade luminal obstruction, with involvement of the proximal or middle segment of the LAD system in about two thirds of patients. In our experience, the latter finding was uniformly lethal in patients undergoing RVOT repair or thromboexclusion of the right ventricle, and clearly represents a contraindication to such decompressive procedures. At present, such patients are better served by providing a secure source of pulmonary blood flow and preserving the pulmonary vasculature in preparation for a modified Fontan procedure.

Thromboexclusion of the right ventricle was performed in a limited number of patients with absent or virtually absent infundibular component of the right ventricle and conspicuous VC connections. This procedure eliminates diversion of coronary diastolic blood flow into the right ventricle through large VC connections, and may mitigate the process of fibrous myointimal hyperplasia and luminal obliteration by prevention of the transmission of suprasystemic right ventricular pressure to the coronary arterial circulation. Although coronary arterial involvement may be advanced in the newborn period, we have seen progression of these lesions postnatally, indicating the potential for therapeutically altering this pernicious process. There are insufficient follow-up data at present to determine the efficacy and the long-term impact of this procedure in patients without obstruction of the proximal left coronary artery and a right ventricle–dependent circulation.

The significant association of a lower right ventricular to left ventricular pressure ratio at the initial cardiac catheterization with reduced postoperative survival reflects an increased risk in patients with severe tricuspid valve insufficiency and Ebstein's malformation of the tricuspid valve or profound tricuspid valve dysplasia. Eleven of 14 patients with Ebstein's anomaly or severe tricuspid valve dysplasia and a grossly dilated right ventricle died in the neonatal period before surgical treatment, and there was only 1 long-term survivor among the remaining 4 surgically treated patients with these morphological features. The spectacular derangement of right ventricular size and function characteristic of pulmonary atresia and intact ventricular septum complicated by Ebstein's anomaly has been emphasized in pathological studies [1, 11].

We currently favor performing a primary transannular RVOT patch repair using a limited period of normothermic bypass for all newborns with pulmonary atresia and intact ventricular septum provided (1) a patent infundibulum of at least moderate size is identified preoperatively and (2) there is no angiographic evidence of obstructive lesions in the proximal left coronary artery. This approach would seem to be the most effective way to relieve right ventricular hypertension, and our preliminary experience suggests that it can be accomplished as safely as closed pulmonary valvotomy. Foker and colleagues [12] reported complete biventricular repair using this protocol in all 10 long-term survivors.

We concur with the strategy advanced by de Leval and associates [13] that atriopulmonary bypass is the procedure of choice for patients with pulmonary atresia and intact ventricular septum who do not attain sufficient right ventricular size and functional capacity to allow complete biventricular repair, provided that such patients are otherwise appropriate candidates for this procedure. The Mayo Clinic experience [14] indicates that RVOT reconstruction can be safely accomplished as a complete repair provided the tricuspid annulus is 70% of normal or greater, a threshold roughly corresponding to two standard deviations below normal and indicative of adequate right ventricular size. The currently used shunt procedures should minimize the risk of pulmonary arterial distortion and preserve the option of a Fontan operation for a much greater proportion of patients with a diminutive tricuspid valve annulus and a globally disadvantaged right ventricle.

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DISCUSSION

DR EDWIN CLIFFORD McGOUGH (Salt Lake City, UT): I congratulate the authors on this comprehensive paper outlining the evolution of the care of children with pulmonary atresia and intact ventricular septum. This report clearly represents the largest series with the longest follow-up to date.

The initial operation to accomplish right ventricular decompression and stabilization of pulmonary blood flow must be evaluated not only in the context of immediate mortality but also in terms of right ventricular growth, successful definitive biventricular repair, and application of the Fontan principle. Dr Coles reports no significant difference in the initial mortality between transannular patching and closed valvotomy and shunting. Perhaps he can tell us the reason for his preference for transannular patching, and also comment on the percentage of patients having valvotomy and shunts who have become suitable candidates for biventricular repair.

Dr Coles and his group are to be congratulated for their results with right ventricular exclusion in the most difficult subset of patients, those with major VC communications.

My associates and I have seen 29 neonates with pulmonary atresia and intact ventricular septum in the last 8 years. Twenty-two of them were deemed candidates for biventricular repair, and they underwent valvotomy and shunting. There were no operative deaths. Seven children with inlet-type ventricles had shunts or a combination of shunts, tricuspid valve excision, and atrial septectomy. There were 2 early and 2 late deaths.

Fourteen of the 22 candidates for biventricular repair have undergone definitive operation, and only one transannular patch was required. There have been no deaths. Doppler pulmonary valve gradients determined at least 2 months after operation have not exceeded 10 mm Hg. Eight patients await repair, and 6 are considered acceptable candidates. Two of the 4 patients with inlet-type ventricles have undergone repair with 1 death. Overall mortality after definitive repair has been 6%, and overall mortality after palliative and definitive repair has been 17%. The 5-year actuarial survival is 86%.

I again congratulate Dr Coles for his fine presentation.

DR COLES: I thank Dr McGough for his comments and congratulate him on a fine series.

Our experience with RVOT reconstruction in newborns was limited to only 12 patients. We favor this approach provided there is a patent infundibulum and no angiographic evidence of obstructive lesions in the proximal left coronary artery. Our enthusiasm for this approach is derived not so much from our own limited experience but from the excellent results achieved by Foker and colleagues [12], who showed good long-term growth potential when the right ventricle was decompressed by an open patch repair using bypass. Other reports have demonstrated the limitations of closed pulmonary valvotomy in terms of right ventricular decompression.

Our experience with excision of the tricuspid valve was limited to 1 patient, and we were unsuccessful in that instance. We have been impressed that the tricuspid annulus is so tiny in these patients that simple excision of the tricuspid valve may not effectively decompress the right ventricle. Rather, we would proceed with thromboexclusion of the right ventricle if the infundibulum is effectively absent, again provided we could exclude the presence of a right ventricle–dependent coronary circulation. The long-term results of this approach are unknown.

Ten Years' Experience With the Senning Operation for Transposition of the Great Arteries: Physiological Results and Late Follow-up

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We report our results in 93 consecutive infants and children who underwent atrial repair of simple transposition of the great arteries using the Senning operation between February 1978 and February 1988. Mean age at operation was 5.6 ± 6.3 months (range, 1 week to 4 years); 60 were less than 6 months old. There were 65 boys and 28 girls. Operative mortality was 5.4%, and there has been 1 late death. Average follow-up is 45.1 months with 39 followed more than 3 years and 25 followed more than 5 years. Postoperative cardiac catheterization was performed in 43 patients. Right ventricular ejection fraction at rest averaged 0.50 ± 0.09 and was normal in 26 patients. Response of right ventricular ejection fraction to afterload stress was abnormal in 12 of 14 patients tested. Right ventricular ejection fraction increased normally during exercise in 6 patients, but was abnormal in 15. Mild tricuspid regurgitation was noted in 10 patients. Mild obstruction of the superior vena cava was noted in 4 patients. Baffle leak requiring reoperation occurred in 1 patient. Seventy-two of 80 patients are in sinus rhythm by latest electrocardiogram. Postoperative electrophysiological studies were performed in 34 patients and Holter monitoring was performed in 22. A major arrhythmia occurred in 8 patients: 3 required a pacemaker for junctional rhythm or sinus node dysfunction, 2 have symptomatic or inducible supraventricular tachycardia, 2 have junctional rhythm, and 1 has sick sinus syndrome. Eight additional patients have delayed sinus node recovery time. At last follow-up, 78 children (97.5%) are in New York Heart Association functional class I, and 2 (2.5%) are in class II. The Senning operation for simple transposition of the great arteries can be accomplished with a low operative mortality. Serious baffle complications requiring reoperation are rare. Surviving patients are clinically well, but arrhythmias and depressed right ventricular function can be a problem with prolonged follow-up.

(Ann Thorac Surg 1989;47:218–23)

Although Senning [1] in 1959 described a repair for simple transposition of the great arteries (TGA) utilizing very little, if any, foreign material to reroute systemic and pulmonary venous return, his method generated little enthusiasm for a variety of reasons, and the Mustard operation was embraced by most surgeons after its introduction in the 1960s. After Quaegebeur and coworkers [2] reported favorable results with the Senning operation in 1977, we began using that operation in February 1978 for all patients seen at the Vanderbilt University Medical Center for repair of simple TGA.

Given the disappointing long-term results in many patients who had the Mustard operation, the increasing numbers of patients seen for transplantation because of right ventricular (RV) dysfunction and arrhythmia, and the recent enthusiasm for the arterial switch operation, we evaluated our 10-year experience with the Senning operation. Although we [3, 4] have reported good early postoperative results with the Senning operation, little information is available on midterm functional results after this procedure. This review is undertaken with an emphasis on late follow-up, evaluation of RV function, and incidence of arrhythmias.

Material and Methods

Patients

Between February 1978 and February 1988, 93 consecutive patients had the Senning repair for simple TGA. Patients with major left ventricular outflow tract obstruction or ventricular septal defect were excluded from this review. Mean age at operation was 5.6 ± 6.3 months (range, 1 week to 4 years), and median age was 5 months. Ninety percent of patients were less than 1 year old (Fig 1). Sixty-five patients were boys and 28 were girls. All patients had undergone a previous balloon atrial septostomy, and 8 patients had had a previous Blalock-Hanlon septectomy.

Data were obtained by review of medical records, cardiac catheterizations, electrocardiograms, Holter monitor recordings, electrophysiological studies, two-dimensional echocardiograms with pulsed Doppler examinations, and written reports from referring cardiologists. Variables are expressed as the mean ± the standard

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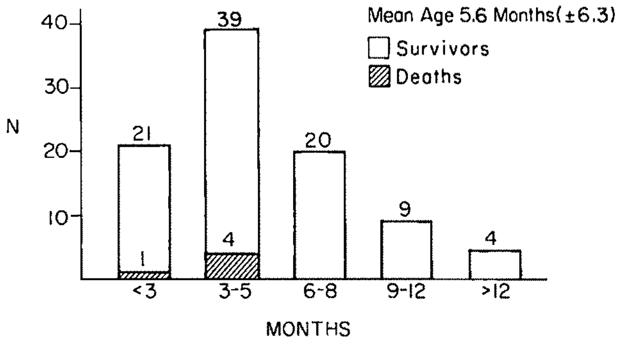

Fig 1. Age at operation. Sixty percent of patients are less than 6 months of age, and 90% are younger than 12 months.

deviation, and actuarial statistics are expressed with 70% confidence intervals. Mortality, morbidity, and actuarial survival data are presented according to guidelines approved by the Council of The Society of Thoracic Surgeons [5]. Actuarial survival statistics were calculated using life-table and survival function software from BMDP Statistical Software, Inc.

Surgical Technique

The operative technique has been described previously and was similar to that presented by Quaegebeur and associates [2]. In infants weighing less than 10 kg who were less than 1 year of age, profound hypothermia and circulatory arrest were used (n = 89). In 4 patients, cardiopulmonary bypass with moderate hypothermia (25°C) was employed. All patients received cold crystalloid cardioplegic solution. Concomitant ligation of the patent ductus arteriosus was carried out in 7 patients, and 2 patients referred from other institutions had takedown of a previously performed systemic–pulmonary artery shunt.

Follow-up

Cardiac catheterization was performed postoperatively in 43 children to assess baffle problems, tricuspid valve regurgitation, and RV function. In 14 patients, work function curves were determined during afterload stress by the method of Borow and associates [6]. Thermodilution cardiac output measurements were made, and RV pressure during systole was measured before and during afterload stress with infusion of phenylephrine hydrochloride or methoxamine hydrochloride. The slope of ventricular work function curves was compared with historical controls [6].

Cardiac rhythm was assessed primarily by electrocardiogram (80 patients), and all Holter studies (22 patients) and electrophysiological studies (34 patients) performed on these patients were reviewed. Functional assessment was based on symptoms, medications, and New York Heart Association grading for patients other than infants.

Right ventricular function was assessed at rest and during supine bicycle exercise by gated equilibrium radionuclide angiography in 21 patients with a normal RV ejection fraction at rest and an average age of 10 years.

Results

Operative Mortality

Mortality within 30 days after operation was 5 (5.4%) of 93 children. Causes of death were myocardial failure (4) and sepsis with multiple-organ failure on postoperative day 20 (1).

Late Mortality

Of 86 survivors, 1 patient died suddenly at another institution 6 weeks postoperatively. Death may have been related to sepsis and acute occlusion of the superior vena cava.

Actuarial analysis of 86 children shows a 5-year and 10-year survival of 93% (confidence limits: 96% and 90%) (Fig 2).

Operative Morbidity

A superficial wound infection that responded to parenteral antibiotics and local wound care developed in 1 patient. Six patients had perioperative seizures, but none have had a subsequent seizure disorder and none require anticonvulsant therapy. Chylothorax developed in the immediate postoperative period in 2 patients, and resolved in both with tube thoracostomy and parenteral nutrition.

Seven patients were lost to follow-up 1 month after discharge from the hospital. These patients were excluded from actuarial survival and arrhythmia analyses, but were not counted as dead in the statistical analyses. Average follow-up in 80 patients was 45.1 months (range, 1 month to 113 months) (Fig 3). Twenty-five patients have been followed for longer than 5 years.

Postoperative Cardiac Catheterization Data

Postoperative cardiac catheterization was performed in 43 patients. Mean cardiac index was 3.58 ± 0.76 L/min/m^2. Mean pulmonary artery pressure was 13 ± 15 mm Hg and pulmonary vascular resistance was 1.8 ± 1.4 U/m^2.

BAFFLE COMPLICATIONS. Angiographic baffle leak was identified in 18 patients, 42% of those undergoing cathe-

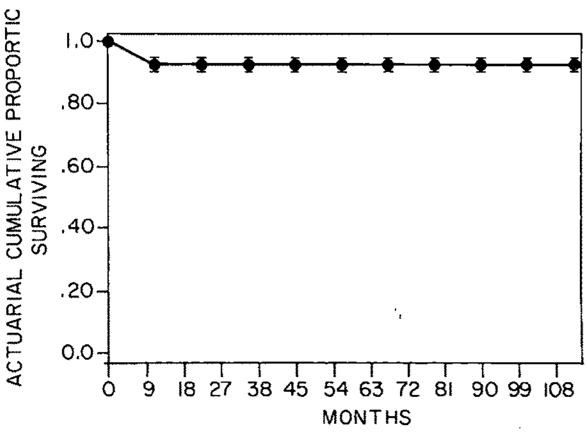

Fig 2. Actuarial survival of patients having the Senning operation. At 5 years and 10 years, survival is 93% (confidence limits: 96% and 90%).

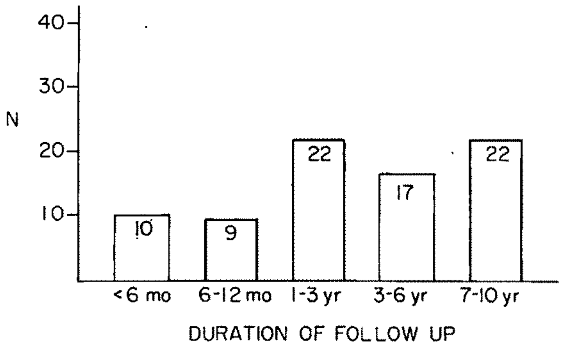

Fig 3. Duration of follow-up. Patients were followed an average of 45.1 months (range, 1 to 113 months). Thirty-nine patients were followed more than 3 years and 25, more than 5 years.

terization. An atrial level shunt was confirmed by oximetry in only 4 patients. The shunt was minimal in 3 patients, but 1 patient required reoperation for a large baffle leak.

Narrowing of the junction between the superior vena cava and the atrium was infrequent. The average gradient between the cava and atrium was 1.4 ± 1.5 mm Hg. No patient had occlusion of the superior vena cava at postoperative catheterization, but in 4 patients the cavoatrial gradient was greater than 3 mm Hg (4, 4, 4.5, and 6 mm Hg). All patients are asymptomatic. In 1 patient who died six weeks postoperatively, acute thrombosis of the superior vena cava was noted at postmortem examination.

Neither inferior vena cava nor pulmonary venous obstruction was encountered.

TRICUSPID REGURGITATION. The patients were evaluated with two-dimensional and pulsed Doppler echocardiography or cardiac catheterization, or both, if any clinical evidence of tricuspid regurgitation was present. Mild tricuspid regurgitation was encountered in 10 patients.

LEFT VENTRICULAR OUTFLOW TRACT OBSTRUCTION. Average left ventricle–pulmonary artery gradient was 10 ± 11 mm Hg. Mild left ventricular outflow tract obstruction (10 to 25 mm Hg) was present in 8 patients, moderate (26 to 49 mm Hg) in 4 patients, and severe (108 mm Hg) in 1 patient. The left ventricle–pulmonary artery gradient was greater than 30 mm Hg in 4 patients (34, 36, 46, and 108 mm Hg).

VENTRICULAR FUNCTION. The average RV systolic pressure was 111 ± 14 mm Hg, and the average diastolic pressure was 9.9 ± 4.6 mm Hg. Right ventricular ejection fraction at rest was 0.50 ± 0.09, and was normal in 26 patients. Normal RV ejection fraction at our institution (mean ± 2 standard deviations) is 0.65 ± 0.16 (range, 0.49 to 0.81). Of the 14 patients evaluated with afterload stress, systemic ventricular work function curves, plotted as ventricular minute work index versus end-diastolic pressure, were abnormal in 12.

Exercise radionuclide ventriculography was performed in 21 patients. All had normal resting RV ejection fractions. Average age of those patients was 10 years, thus representing long-term follow-up in all patients. Right ventricular ejection fraction increased normally in only 6. Ejection fraction actually fell during exercise in 4 patients, and failed to increase in the remaining 11.

Table 1. Postoperative Rhythm Status

Finding	No. of Patients
Sinus rhythm	72
Junctional rhythm	4
Sick sinus syndrome	1
Sinus bradycardia	1
Supraventricular tachycardia	2
Wandering atrial pacemaker	2
Sinoatrial node dysfunction	8
Pacemakers	3

Postoperative Rhythm Status

Late electrocardiographic follow-up data were available for 80 patients. Seventy-two (90%) are in sinus rhythm by the latest electrocardiogram. Three patients required pacemakers for junctional rhythm (2) or sinus bradycardia (1). Two patients have symptomatic or inducible supraventricular tachycardia. Two additional patients have junctional rhythm, and 1 has sick sinus syndrome (Table 1, Fig 4).

Holter recordings were made in 22 patients. Sinus rhythm was a predominant rhythm in the majority of patients (12/22). However, wandering atrial pacemaker was seen in 2, and brief asymptomatic episodes of junctional rhythm were noted in 7 patients. Junctional rhythm was confirmed in 2 patients and sinus bradycardia in 1. Ventricular arrhythmias were rarely seen.

Thirty-four patients had electrophysiological studies either at cardiac catheterization 1 year postoperatively or immediately before discharge postoperatively using tem-

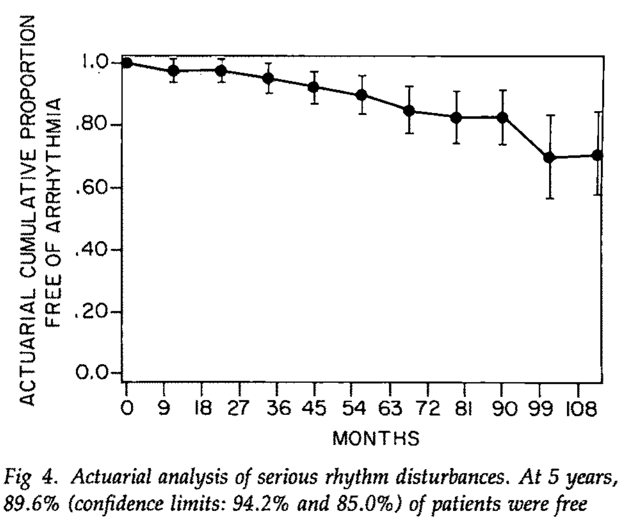

Fig 4. Actuarial analysis of serious rhythm disturbances. At 5 years, 89.6% (confidence limits: 94.2% and 85.0%) of patients were free from arrhythmias, but only 69.8% (confidence limits: 82.1% and 57.5%) were free from arrhythmias at 10 years.

porary epicardial pacing wires. Four studies were performed to investigate symptomatic arrhythmia, and 30 were considered screening evaluations. Abnormal sinus node recovery time was identified in 8 patients, and subtle atrioventricular node abnormalities were encountered in 4.

Actuarial analysis of arrhythmias demonstrates increasing frequency with time and no evidence of a plateau (see Fig 4). Although approximately 90% of patients are free from serious rhythm disturbance, defined as junctional rhythm, supraventricular tachycardia, and bradycardia requiring a pacemaker after 5 years (confidence limits: 94% and 85%), only 70% remain so after 10 years (confidence limits: 82% and 58%).

Functional Status

Of 80 patients available for late follow-up, the majority (78 or 97.5%) are in New York Heart Association functional class I, and 2 patients with moderate RV dysfunction are in class II. Ninety-seven percent were receiving no medication. Two patients were receiving digoxin for arrhythmia management. No patient is in New York Heart Association class III or IV.

Comment

Atrial repair of simple TGA can be accomplished in infancy with low operative mortality [3, 4, 7–14]. The Senning operation utilizes very little, if any, foreign material to reroute systemic and pulmonary venous return, thereby optimizing the potential for atrial growth and contraction. We have been pleased with the low frequency of major caval obstruction and the absence of pulmonary venous obstruction in this series, compared with our own experience as well as that of others with the Mustard operation [10–12, 15]. In the series of patients having the Mustard operation from Toronto [7], vena caval stenosis or pulmonary venous stenosis was present in 24.6% of 126 patients undergoing recatheterization. In fact, baffle complications in patients having the Mustard procedure for atrial repair led to death or reoperation in 19 patients or 6% of 316 early survivors.

Operative mortality for both the Senning and the Mustard operation is low: 1% to 5% [3, 4, 7–13]. In addition, survival statistics to 10 years, and even 20 years with the Mustard operation, are excellent, with up to 95% of children surviving 10 years. The greater issue, however, as the early results with arterial repair for simple transposition in the neonatal period are becoming competitive with atrial repair [9], is the long-term results with respect to systemic ventricular function and arrhythmias.

In our series, midterm survival is excellent, with 10-year survival of 93% (confidence limits: 96% and 90%). As with the Mustard operation, however, arrhythmias continue to be a major problem [7, 15, 16]. By actuarial analysis, only 69.8% ± 12.3% of patients are free from serious rhythm disturbance 10 years postoperatively, and less serious conduction disturbances are present in 17 (21.2%) of 80 survivors.

Postoperative systemic ventricular function is a major concern after atrial or arterial repair of TGA. Clinical results are gratifying in that the majority of patients, 97.5% in our series, are unrestricted and asymptomatic, and appear able to keep up with their peers. However, detailed exercise testing of other children after atrial repair of TGA has determined that exercise performance [17] and exercise tolerance [18] are diminished compared with normal children.

Objective evaluation of RV function, either early postoperatively with afterload stress or late postoperatively with exercise radionuclide ventriculography, however, presents a different picture. Our early results, as well as those of Borow and colleagues [6], show an abnormal RV response to afterload stress in the majority of patients at the time of catheterization 1 year postoperatively. Evaluation of RV function 10 years postoperatively in these patients confirms what other investigators have noted after atrial repair of TGA: 60% to 70% have an abnormal response to exercise. Twenty percent to 30% actually have a decline in RV ejection fraction with exercise [6, 18–24]. Our series is unique in that all 21 patients tested with exercise radionuclide ventriculography have normal resting ejection fractions and are asymptomatic.

This evaluation is not intended to compare the results of the Senning operation with other repairs, but to evaluate our 10 years' experience and to provide medium-term and some long-term information on these children. We are concerned that serious rhythm disturbances are becoming more frequent as time passes postoperatively, and may contribute to late mortality or morbidity, currently absent in our series. Although the ultimate importance of an abnormal RV response to afterload stress and exercise is not known, we are uneasy about the prevalence of abnormal exercise responses at the 10-year follow-up.

The arterial switch operation is appealing, as one would anticipate less long-term morbidity with arrhythmias, systemic atrioventricular valve incompetence, and ventricular dysfunction. Our limited early experience with the arterial repair of simple TGA in the neonate confirms a low early mortality that is competitive with the mortality of atrial repairs. Although we have not abandoned the Senning operation, our current operation of choice for simple TGA in the newborn is arterial repair.

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DISCUSSION

DR CONSTANTINE MAVROUDIS (Louisville, KY): I congratulate the authors on a well-researched, well-presented, and well-executed series on the midterm follow-up of patients who had a Senning operation for TGA with intact ventricular septum.

The introduction of the arterial switch operation has resulted in numerous debates concerning the ideal operation for these babies. This study accurately documents the pertinent hemodynamic course of these patients and serves as an excellent study with which to describe any further studies.

Outcome for any procedure for transposition must assess the success from birth to the time of operation, and obviously thereafter. The difficulty with this and other studies like it is that we do not know how many patients died waiting the 3 to 6 months for the definitive operation. Although these patients do not represent operative deaths, their deaths are due to the system. Can the authors give us data on this group of patients who were born with transposition but died waiting for the operation?

The arterial switch operation does not create this system problem, as all babies are operated on within the first week of life. Over the last 3 years, we have performed 36 arterial switch operations with 4 deaths, an 11% mortality, which is comparable to that in high-volume centers, which have reported a mortality ranging between 8% and 12%. All our patients have normal sinus rhythm, and only 1 has required reoperation for pulmonary stenosis.

As the mortality rate for the arterial switch operation approaches that for atrial repair, the enthusiasm for this operation will increase. Accordingly, long-term studies like this one will show us the efficacy of each procedure. Have the authors implemented a system to follow patients with transposition from birth, thereby being able to tell us what has happened to these patients while awaiting operation?

DR BENDER: I thank Dr Mavroudis for his nice comments and will attempt to answer the very difficult question that he poses.

I certainly agree that to assess results of any operative repair in transposition or any congenital malformation, you need to know what happens to the total population of patients and not just those patients on whom you've operated. It's impossible for us to know what has happened to all patients seen in all institutions that have subsequently referred patients to us for treatment of transposition. We do know that at the time we looked at these data, we had 93 patients who underwent atrial repair. In all, 117 patients with transposition had been seen at Vanderbilt. Several of them were waiting for subsequent atrial repair, and none of those patients died while awaiting this subsequent repair. I do not know whether there were deaths among patients in other institutions who had had atrial septostomy and had not been referred to us.

As Dr Stewart mentioned, we have been pleased with the results in these children clinically. They are doing well, they look well, and they and their parents believe they compare reasonably well with their peers.

I'm very concerned about the abnormal exercise data and stress data with respect to RV function, and I'm concerned about the steadily increasing numbers of arrhythmias as we follow these children. As mentioned earlier, we no longer do this procedure for patients with simple transposition who are seen by us initially. For the last 1.5 years, we've been doing the arterial switch as our primary treatment for simple transposition, and to date we have no deaths among those patients. We will continue to follow both groups of patients as they grow up.

Notice From The Society of Thoracic Surgeons

The Society of Thoracic Surgeons is pleased to announce two new membership categories, International and Candidate, with the following qualifications.

International Members: Members of this category shall reside outside the United States and Canada. Their training in this specialty shall be considered equivalent to that of active members. They shall have achieved appropriate certification or recognition of their achievements in this specialty in their country and must devote the majority of their professional efforts in the interests of the specialty. Appropriate documentation of professional achievements shall be provided to the Membership Committee. Members residing in countries other than the United States and Canada elected to membership before October 1, 1988, shall maintain their current status until eligible for Senior Membership or Inactive Status. The dues will be similar to those charged for Active Members.

Candidate Members: Members of the Candidate Group shall be enrolled in a thoracic and cardiovascular training program accredited by the Residency Review Committee for Thoracic Surgery under the authority of the Accreditation Council for Graduate Medical Education or in a similar program approved for training by the Royal College of Surgeons of Canada. Also, individuals who have completed their training in one of the above programs and are in the process of acquiring certification by the American Board of Thoracic Surgery or the Royal College of Surgeons of Canada are eligible for this type of membership. Upon obtaining and presenting appropriate qualifications for active membership, a member of the Candidate Group, upon request and recommendation of the Membership Committee, Council, and membership, shall be advanced to this category in The Society and shall become subject to all of the responsibilities, rights, duties, assessments, and privileges of an Active Member. Membership in the Candidate Group will be for a maximum of 5 years following completion of training. The annual dues are $55.

Dues for both groups include a subscription to *The Annals of Thoracic Surgery*. The 1989 application deadline is May 1st. Applications for both types of membership are available from The Society of Thoracic Surgeons, 111 East Wacker Drive, Suite 600, Chicago, IL 60601; telephone (312) 644-6610.

Continued Assessment of the Combined Collis-Nissen Operation

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The combined Collis-Nissen operation has been performed in 353 patients. Forty-five percent had reflux esophagitis without stricture; 20%, peptic stricture; 72%, a sliding hiatal hernia; 17%, a paraesophageal hernia; 21%, previous antireflux operation; 15%, esophageal spasm; 8%, scleroderma; and 32%, marked obesity. There were 4 postoperative deaths (mortality rate, 1.1%). Complications occurred in 28 patients (8%) and included wound infection (2.2%), esophageal or gastroplasty tube leak (1.7%), bleeding (1.1%), splenic injury, gastric atony, and crural repair dehiscence (each less than 1%). Follow-up includes personal interview, esophageal manometry, and standard acid reflux testing. The average length of follow-up for 261 patients (74%) followed at least 12 months is 43.8 months. Fifty-eight percent have been followed at least 36 months; 41%, 48 months; and 29%, 60 months or longer. Subjectively, in these 261 patients, reflux has been eliminated in 75%, is mild in 11%, is moderate in 9%, and is severe in 5%. Eight percent have postthoracotomy pain; 3%, early satiety ("bloats"); and 1%, postvagotomy diarrhea. Seventeen percent require either periodic or regular esophageal dilations for dysphagia. Objectively, intraesophageal pH studies show good reflux control in 91% and poor reflux control in 9%. Twenty-six patients (10%) have required reoperation for recurrent reflux or dysphagia. These results substantiate satisfactory reflux control using the Collis-Nissen operation in patients at risk for recurrence after standard repairs, but also emphasize that, like other antireflux procedures, the Collis-Nissen operation is not without some degree of postoperative adverse symptoms.

(Ann Thorac Surg 1989;47:224–30)

The goal of antireflux operations is to prevent gastroesophageal reflux and its major complications—stricture and aspiration—without causing new adverse symptoms. Unsatisfactory results occur when reflux is inadequately controlled or when major new symptoms such as dysphagia or gas bloat syndrome result from the repair itself. Published reviews [1–6] indicate that reflux is controlled in 85% to 90% of patients after operation, but that additional untoward symptoms, not necessarily related to reflux, develop in 10% to 25%.

Since late 1976, the Collis-Nissen operation has been the procedure of choice in most of the patients having an antireflux operation at the University of Michigan Medical Center [7]. The previous experience at our institution [8, 9] as well as that at others [10, 11] has shown that a complete fundoplication provides better reflux control than a partial gastric wrap, particularly after construction of a Collis gastroplasty. The esophageal lengthening Collis gastroplasty [12] facilitates a tension-free repair and provides a resilient gastric tube around which to perform the fundoplication, thereby eliminating the need to place sutures into the inflamed esophageal wall. This report updates the earlier reported experience of Orringer and Orringer [9] with the Collis-Nissen operation and further evaluates its efficacy in the long-term control of gastroesophageal reflux.

Material and Methods

The medical records of 353 patients who underwent the Collis-Nissen operation between August 1976 and June 1988 on the University of Michigan Thoracic Surgery Service were reviewed retrospectively. One hundred eighty-two (52%) were men, and 171 (48%) were women. Their average age was 51 years (range, 17 to 94 years). Marked obesity was present in 112 patients (32%) and scleroderma in 28 (8%). Seventy-five patients (21%) had undergone previous antireflux operations, and 10 (3%) had had previous ulcer operations, including vagotomy with antrectomy or pyloroplasty.

Heartburn was the most common symptom; it was experienced by 304 patients (86%). Regurgitation was experienced by 263 patients (75%). Some degree of dysphagia was present in 202 patients (57%), and was graded as mild (requiring no dilations) in 122 (35%), moderate (requiring occasional dilations) in 57 (16%), and severe (requiring regular dilations) in 23 (7%). Other symptoms included aspiration in 72 patients (20%), esophageal spasm in 53 (15%), gastrointestinal bleeding in 39 (11%), and weight loss greater than 4.54 kg in 37 (10%).

Preoperative barium esophagograms were obtained routinely. Of the 334 studies available for review, 239 patients (72%) had a sliding hiatal hernia, and gastroesophageal reflux was seen radiographically in 111 (33%).

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Fifty-seven patients (17%) had a paraesophageal component to the hiatal hernia. Distal esophageal narrowing was seen in 70 patients (21%).

Preoperative endoscopy was performed in 346 patients (98%). Some degree of endoscopic esophagitis was present in 226 (65%): grade I (erythema) in 59 (17%), grade II (ulceration) in 96 (28%), and grade III (ulceration with dilatable stricture) in 71 (21%). No esophagitis was seen in 120 patients (35%). In 29 patients (8.2%), Barrett's epithelium was diagnosed by biopsy or by characteristic endoscopic findings.

Esophageal function tests, including manometric and standard intraesophageal acid reflux testing, as described previously [13], were performed in 316 patients (90%) preoperatively. Abnormal (2 to 3+) acid reflux was documented in 282 (89%). Average peak pressure in the distal esophageal high-pressure zone was 4.0 ± 5.1 mm Hg, and length of the high-pressure zone averaged 1.7 ± 1.9 cm.

The indications for operation included the presence of a paraesophageal hernia (57 patients) or failure of medical antireflux therapy with persistent symptoms or esophagitis. Our technique for the combined Collis-Nissen operation has been described [7], as have our more recent modifications [14]. In our first 235 patients, the gastroplasty tube was constructed over a dilator in the 54F to 60F range. This dilator was then removed and replaced with a 46F bougie around which a 6-cm fundoplication was performed, partly around the proximal stomach and then the distal gastroplasty tube. In our last 118 patients, we have used a 54F dilator in women and a 56F dilator in men for construction of both the gastroplasty and the fundoplication. Further, in an effort to reduce postoperative dysphagia, the fundoplication has been limited to 3 cm in length and encircles only the distal gastroplasty tube.

Nineteen patients (5%) required diaphragmatic counterincisions and 2 patients (0.6%) required thoracoabdominal incisions to permit adequate gastric mobilization after previous hiatal hernia or ulcer operations. Pyloromyotomy through a separate abdominal incision was performed in 16 patients (4.5%) because of uncertainty about the integrity of the vagus nerves after esophageal mobilization. Twenty-seven of the 53 patients with esophageal spasm underwent concomitant long esophagomyotomy.

Postoperatively, patients were followed with personal interview, esophageal manometry, and the standard acid reflux test. The results of the Collis-Nissen operation were assessed in terms of objective reflux control, subjective reflux control, postoperative dysphagia, and overall clinical status (reflux and dysphagia symptoms) for patients with follow-up longer than 12 months.

Differences between groups of patients were compared with χ^2 analysis or Fisher's exact test where appropriate. The following variables were assessed to determine their effect on clinical outcome: age greater than 70 years, obesity, spasm, scleroderma, previous antireflux operation, presence of peptic stricture, presence of a paraesophageal hernia, Barrett's epithelium, and technique of operation (3-cm wrap with 54F to 56F dilator versus 6-cm wrap with 46F dilator).

Results

There were 4 postoperative deaths (1.1% operative mortality), 1 each due to pulmonary embolus, aspiration pneumonia, leak from an esophagomyotomy, and small bowel obstruction. Complications occurred in 28 patients (7.9%). Wound infection was the most common complication (8 patients). Leaks occurred in 6 patients, in 2 from the Collis gastroplasty tube and in 4 from the distal esophagus or proximal stomach. Other complications included postoperative hemorrhage requiring reoperation (4 patients), splenic injury requiring splenectomy (2 patients), early postoperative crural dehiscence (2 patients), gastric atony (2 patients), small bowel obstruction (1 patient), pulmonary embolus (1 patient), chylothorax (1 patient), and aspiration pneumonia (1 patient). The postoperative hospitalization averaged 9.5 days for the 349 operative survivors.

The average length of follow-up for 261 patients (74%) followed at least 12 months is 43.8 months (range, 12 to 132 months), and all subsequent results apply to these 261 patients. One hundred ninety-four (74%) have been followed for at least 24 months, 151 (58%) for at least 36 months, 106 (41%) for at least 48 months, and 76 (29%) for at least 60 months.

Average postoperative distal peak pressures in the high-pressure zone ranged from 10.3 ± 4.1 mm Hg to 11.5 ± 3.6 mm Hg, clearly increased from the preoperative value of 4.0 ± 5.1 mm Hg (Table 1). Likewise, high-pressure-zone length was increased after operation, with mean lengths ranging from 3.5 ± 1.1 cm (36 months) to 4.4 ± 1.1 cm (48 months) compared with the preoperative length of 1.7 ± 1.9 cm. At the time of most recent follow-up, good reflux control was demonstrated by the standard acid reflux test in 215 (91%) of the 237 patients studied (Table 2). However, 8 of the 215 patients with good reflux control as determined by the standard acid reflux test were found to have abnormal reflux with 24-hour intraesophageal pH monitoring. Eight of the 22 patients with poor objective reflux control by the standard acid reflux test have no symptoms of gastroesophageal reflux.

Satisfactory symptomatic control of gastroesophageal reflux (no symptoms or mild symptoms not requiring treatment) was achieved in 86% of the patients (see Table 2). To facilitate further analysis, the patients were subdivided into two groups, complicated (spasm, scleroderma, previous antireflux operation, stricture, or paraesophageal hernia) and uncomplicated (none of the previous features). Reflux symptoms were satisfactorily controlled in 91% of the uncomplicated group compared with 84% of the complicated group, but this difference did not reach significance ($p > 0.05$).

Dysphagia was absent or mild (not requiring treatment) in 83% of the patients postoperatively (see Table 2). Twenty-one (8%) currently require occasional dilations for dysphagia, and 23 (9%) require regular dilations. Persistent dysphagia requiring dilation was significantly more likely in patients from the complicated group than the uncomplicated group (22% versus 4%; $p < 0.05$).

Persistent postthoracotomy pain was experienced by 20

Table 1. Collis-Nissen Esophageal Function Tests[a]

Time	No. of Patients Examined	HPZ Pressure (mm Hg)	HPZ Length (cm)	Abnormal Acid Reflux	
				No.	%
Preoperative	316	4.0 ± 5.1	1.7 ± 1.9	282	89
Postoperative (mo)					
12	216	11.5 ± 3.6	4.3 ± 1.1	9	4
24	131	11.0 ± 3.4	4.2 ± 1.0	14	11
36	95	10.3 ± 4.1	3.5 ± 1.1	8	8
48	63	10.7 ± 2.9	4.4 ± 1.1	11	17
60	43	10.8 ± 3.6	4.0 ± 1.1	4	9

[a] This table presents the total data for all patients examined at each follow-up interval.

HPZ = high-pressure-zone.

patients (7.6%). Eight patients (3%) had mild early satiety ("bloats"), and 3 (1%) experienced postoperative diarrhea.

The overall subjective clinical status was excellent (no symptoms) in 132 patients (51%), good (mild symptoms not requiring treatment) in 63 (24%), fair (reflux symptoms or dysphagia controlled by medical therapy or dilation) in 34 (13%), and poor (severe, uncontrolled symptoms) in 32 (12%) (see Table 2). Thus, the Collis-Nissen operation was successful (no symptoms or mild symptoms not requiring treatment) in 75% of the patients. A satisfactory result was significantly ($p < 0.05$) more likely in the uncomplicated group (87%) than the complicated group (70%). Postoperative dysphagia was more commonly the reason for an unsatisfactory result than recurrent reflux. Despite the fact that they met our criteria for an unsatisfactory result, 12 of the 66 patients with unsatisfactory results thought that their condition was clearly improved by the Collis-Nissen operation.

Certain types of esophageal pathology clearly influenced clinical outcome (Table 3). Patients with spasm were more likely ($p < 0.05$) to have dysphagia and an unsatisfactory clinical outcome. Scleroderma was associated ($p < 0.05$) with poor objective reflux control, unsatisfactory subjective reflux control, postoperative dysphagia, and an unsatisfactory overall clinical outcome. Patients with previous antireflux operations were more likely ($p < 0.05$) to have unsatisfactory subjective results (subjective reflux, dysphagia, and overall clinical status) than patients without previous antireflux procedures. Although patients with strictures had poorer ($p < 0.05$) objective reflux control than patients without strictures and more dysphagia ($p < 0.05$) than patients in the uncomplicated group, they did not have a significantly

Table 2. Collis-Nissen Results at Most Recent Follow-up

Group	Acid Reflux Test (n = 237)		Reflux Symptoms[a] (n = 261)				Dysphagia[b,c] (n = 261)				Clinical Status[d,c] (n = 261)			
	Normal (0–1+)	Abnormal (2–3+)	None	Mild	Moderate	Severe	None	Mild	Moderate	Severe	Excellent	Good	Fair	Poor
Total (n = 261)														
No.	215	22	195	29	24	13	152	65	21	23	132	63	34	32
%	91	9	75	11	9	5	58	25	8	9	51	24	13	12
Uncomplicated[e] (n = 77)														
No.	66	6	62	8	4	3	62	12	2	1	52	15	5	5
%	92	8	81	10	5	4	81	16	3	1	68	19	6	6
Complicated[f] (n = 184)														
No.	149	16	133	21	20	10	90	53	19	22	80	48	29	27
%	90	10	72	11	11	5	49	29	10	12	43	26	16	15

[a] The grading for reflux is as follows: mild = requires no treatment; moderate = controlled by medical therapy; severe = uncontrolled by medication or need for reoperation. [b] The grading for dysphagia is as follows: mild = requires no dilation; moderate = requires occasional dilation; severe = requires regular dilation or reoperation. [c] Significance: $p < 0.05$, uncomplicated group compared with complicated group. [d] The grading for clinical status is as follows: excellent = asymptomatic; good = minimal reflux symptoms or mild dysphagia requiring no treatment; fair = symptoms controlled by medication or dilation; poor = symptoms severe or reoperation required. [e] Uncomplicated means patients without spasm, scleroderma, previous antireflux operation, stricture, or paraesophageal hernia. [f] Complicated means patients with any of the following: spasm, scleroderma, previous antireflux operation, stricture, or paraesophageal hernia.

Table 3. Esophageal Pathology and Clinical Outcome[a]

	Acid Reflux Test		Reflux Symptoms		Dysphagia		Clinical Outcome	
Patient Group	Normal (0–1+)	Abnormal (2–3+)	Satisfactory[b]	Unsatisfactory[c]	Satisfactory[b]	Unsatisfactory[c]	Satisfactory[b]	Unsatisfactory[c]
Uncomplicated[d] (n = 77)	66 (92)	6 (8)	70 (91)	7 (9)	74 (96)	3 (4)	67 (87)	10 (13)
Spasm (n = 43)	38 (95)	2 (5)	36 (84)	7 (16)	28[e,f] (65)	15[e,f] (35)	26[e,f] (60)	17[e,f] (40)
Scleroderma (n = 26)	18[e] (78)	5[e] (22)	14[e,f] (54)	12[e,f] (46)	16[e,f] (62)	10[e,f] (38)	11[e,f] (42)	15[e,f] (58)
Reoperation (n = 53)	42 (93)	3 (7)	40[e,f] (75)	13[e,f] (25)	31[e,f] (58)	22[e,f] (42)	27[e,f] (51)	26[e,f] (49)
Stricture (n = 55)	41[e] (80)	10[e] (20)	46 (84)	9 (16)	44[f] (80)	11[f] (20)	42 (76)	13 (24)
Paraesophageal hernia (n = 44)	33 (94)	2 (6)	43[e] (98)	1[e] (2)	40 (91)	4 (9)	39[e] (89)	5[e] (11)

[a] Numbers in parentheses are percentages. [b] Satisfactory means no symptoms or mild symptoms not requiring treatment. [c] Unsatisfactory means symptoms requiring treatment with medication, dilation, or reoperation. [d] Uncomplicated means no spasm, scleroderma, reoperation, stricture, or paraesophageal hernia. [e] Significance: $p < 0.05$ compared with all patients without the indicated pathology. [f] Significance: $p < 0.05$ compared with uncomplicated group.

greater likelihood of unsatisfactory subjective reflux control or unsatisfactory overall clinical results. Five (63%) of 8 patients with strictures after failed antireflux operations had an unsatisfactory overall clinical outcome. An overall satisfactory clinical outcome was achieved in 39 (83%) of the 47 patients with strictures but without previous antireflux operations. The presence of a paraesophageal hernia was not a risk factor for an unsatisfactory result.

The clinical results have been influenced by the recent modifications in our technique for the Collis-Nissen operation (Table 4). Subjective reflux control has improved ($p < 0.05$), as has overall clinical status. The incidence of postoperative dysphagia is also less with our current technique, but this difference does not reach significance ($p > 0.05$). The presence of obesity, advanced age (greater than 70 years), or Barrett's epithelium had no significant ($p > 0.05$) effect on clinical outcome.

Twenty-six of the 32 patients with poor results after the Collis-Nissen operation have undergone reoperation for symptoms of reflux or dysphagia. The Collis-Nissen operation has been revised in 3 patients, and 2 patients have had repair of a paraesophageal hiatal hernia caused by late crural disruption, all with subsequent good or excellent results. Transhiatal esophagectomy without thoracotomy and cervical esophagogastrostomy has been performed in 18 patients. One patient each has undergone esophagogastrectomy with intrathoracic esophagogastrostomy, distal esophagectomy and short-segment colon interposition, and division of scar tissue at the diaphragmatic hiatus.

Comment

The Collis gastroplasty lengthens the functional esophagus and provides a healthy tube of stomach around which to perform a fundoplication. In so doing, tension on the repair is avoided, and the need for the tenuous esophageal sutures of a standard fundoplication is eliminated. Theoretically, these advantages of the combined Collis-Nissen operation should minimize the chance of poor reflux control, particularly in patients at increased risk for recurrence after standard repairs—those with severe esophagitis, periesophageal inflammatory reaction, reflux stricture, esophageal shortening, marked obesity, and chronic obstructive pulmonary disease.

The ultimate effectiveness of an antireflux operation

Table 4. Effects of Modification of Collins-Nissen Operation[a]

	Previous Technique[b] (n = 196)				Current Technique[c] (n = 63)			
	Satisfactory[d]		Unsatisfactory[e]		Satisfactory[d]		Unsatisfactory[e]	
Variable	No.	%	No.	%	No.	%	No.	%
Acid reflux test	159	90	18	10	56	93	4	7
Reflux symptoms[f]	162	83	34	17	60	95	3	5
Dysphagia	160	82	36	18	55	87	8	13
Clinical status[g]	141	72	55	28	53	84	10	16

[a] Numbers in parentheses are percentages. [b] Previous technique was 6-cm wrap over 46F dilator. [c] Current technique is 3-cm wrap over 54F to 56F dilator. [d] Satisfactory means no symptoms or mild symptoms not requiring treatment; normal acid reflux test. [e] Unsatisfactory means symptoms requiring medical therapy, dilation, or reoperation; abnormal acid reflux test. [f] Significance: $p < 0.05$ for differences between previous technique and current technique. [g] Significance: $p = 0.0523$ by χ^2 analysis and $p = 0.0349$ by Fisher's exact test, previous technique compared with current technique.

must be judged on the basis of long-term subjective and objective clinical results. In a previous report [9], an initial assessment of the Collis-Nissen operation in providing reflux control in a group of 135 patients followed for an average of 24 months was presented. In this report, the results in 261 patients followed for an average of 43.8 months are reviewed. In this current evaluation of the Collis-Nissen operation, stringent and rigid criteria have been imposed to define subjective results, and routine postoperative esophageal function tests have been utilized. Only 9% of our patients have objective pH probe evidence of abnormal reflux, in contrast to our results with the Collis-Belsey operation (30% abnormal reflux after an average follow-up of only 13 months) [8]. Subjective reflux control has been achieved in 91% of our uncomplicated group (93% if paraesophageal hernias are included in the uncomplicated group), which is comparable to the results of others [15–17] using the Nissen fundoplication with or without gastroplasty. These results substantiate satisfactory reflux control using the Collis-Nissen operation in patients judged to be at risk for recurrence after standard repairs.

Any operation designed to augment lower esophageal sphincter pressure has the potential for producing postoperative dysphagia. However, neither the incidence nor the severity of dysphagia is carefully analyzed in most reviews of antireflux operations. This is a serious oversight. Our 4% incidence of dysphagia necessitating dilation postoperatively in the uncomplicated group is similar to the experience of DeMeester and associates [17] with a short Nissen wrap. Our complicated group had a much higher incidence of major postoperative dysphagia (10% requiring occasional dilations and 12% requiring regular dilations). Pearson and associates [18] found an 11% incidence of dysphagia in a similar group of patients treated with the Collis-Belsey operation.

Five years ago, we began to construct a shorter Nissen wrap over a larger dilator with the intent of decreasing postoperative dysphagia. We now limit the length of the fundoplication to 3 cm and wrap only the distal gastroplasty tube and not the proximal stomach as Orringer and Sloan [7] initially described. Results with this modification appear promising. Dysphagia is decreased (although the decrease does not reach statistical significance), and subjective reflux control is improved. It is too early, however, to draw firm conclusions about the efficacy of this technique; additional long-term follow-up of these patients is needed. We are encouraged by the fact that DeMeester and associates [17] also noted improved results after reducing the length of the fundoplication.

As we [19] and others [20] have previously reported, a history of a previous antireflux operation is a significant risk factor for an unsatisfactory result from another such procedure. It is disturbing that the Collis-Nissen operation produced overall unsatisfactory results in nearly half (49%) of our patients with previous repairs. It should be emphasized, however, that these poor results were more often due to persistent postoperative dysphagia than to inadequate reflux control. Nevertheless, these results are unacceptable. It is hoped that the recent modifications in the Collis-Nissen operation (shorter wrap over a larger dilator) will lead to improved results and a lower incidence of dysphagia. As we have reported [14], patients with strictures after failed antireflux operations are more likely to have an unsatisfactory result after the Collis-Nissen operation than patients with strictures and no prior repair. However, stricture in the absence of a previous antireflux operation is not a risk factor for a poor overall clinical outcome.

Scleroderma and diffuse esophageal spasm are clearly risk factors for a poor result after antireflux operations. Although gratifying initial palliation of reflux symptoms in the patient with scleroderma can be achieved [21], the fundoplication must be short and loose to prevent esophageal obstruction. Progressive esophageal neuromotor dysfunction, the need for frequent dilations even in the absence of a stricture, and recurrent reflux symptoms are ultimately responsible for a poor operative result in these patients. The patient with primary esophageal spasm has a functional bowel disease and, generally, an easily recognized psychosomatic personality. The operative treatment of psychiatric disease is less than gratifying, and we have virtually abandoned esophagomyotomy as a therapeutic option in these patients, who frequently continue to complain of chest pain and dysphagia postoperatively. In those with gastroesophageal reflux requiring an operation, if there is concomitant esophageal spasm, the patient is informed that the complaints of chest pain and intermittent dysphagia may persist after the antireflux procedure. Most such patients do not have esophageal muscular hypertrophy at operation, and no esophagomyotomy is performed with the fundoplication. If marked muscular hypertrophy is found, however, an esophagomyotomy is carried out with a modified Belsey procedure (240-degree wrap) to minimize postoperative dysphagia.

The operative treatment of gastroesophageal reflux remains a challenge, and the variety of approaches to this problem advocated in the surgical literature suggests that the "ideal" has yet to be established. Even in the best of hands, a substantial number of patients, particularly those with complicated esophageal disease, will have unsatisfactory results because of both recurrent or persistent reflux and dysphagia. Careful long-term follow-up with meticulous analysis of subjective and objective results is essential if the results of antireflux operations are to be meaningfully and intelligently compared and improved in the future.

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DISCUSSION

DR F. G. PEARSON (Toronto, Ontario, Canada): Mr Ronald Belsey in his inimitable and colorful fashion has frequently made the statement: "The battlefields of surgery are littered with the remains of new operations. Early spectacular results fade away in the rooms and corridors of the follow-up clinic." These words are certainly never more appropriate than with reference to antireflux surgery. I compliment Drs Stirling and Orringer on their critical analysis, with objective and subjective evaluation, of the long-term follow-up of 261 patients with a variety of reflux pathologies who have been managed by gastroplasty and the Nissen fundoplication, a group of patients who have been followed since this series began 12 years ago.

Furthermore, this evaluation includes a statistical analysis of a number of potentially important risk factors, observations that are not available in many prior reports. Of their patients, 261 have now been followed for more than a year, with an average follow-up of 44 months, and 76 patients have been followed for at least 5 years. Overall, good results were obtained in 75% of patients. Unsatisfactory results were due to persistent or recurrent reflux in a relatively small number of patients (9%), but were due to dysphagia requiring periodic or regular dilations in a disturbingly high number of patients (17%). The incidence of persistent postoperative dysphagia has been addressed by the authors, and they hope to improve results by modifying the technique of repair with a larger-diameter gastric tube and a shorter length of fundoplication.

Postoperative dysphagia is always a potential problem with a complete fundoplication. It is one of the reasons that some of us favor a partial fundoplication in many cases.

The data presented identify some specific significant risk factors that adversely affect the prognosis, motor disorders and repeat operations in particular. The incidence of unsatisfactory results with reoperation in this series is almost 50%, and it is similar for motor disorders. In evaluating the overall percentage of satisfactory results, the presence of a peptic stricture was not identified as a risk factor, nor were obesity, advanced age, or paraesophageal hernia. Our own follow-up data from a recent review concur with these observations.

In a review of our patients now followed for almost 25 years with a prospective protocol, there are 250 patients who have been followed for longer than 5 years and 100 patients who have been followed for more than 10 years. For patients with peptic stricture and esophagitis but without an underlying motor disorder and no prior operation, there is a high percentage of satisfactory results (93%). But the good results certainly diminish with repeat operations (79%) and markedly decrease in the presence of an associated primary motor disorder (51%).

I would like to emphasize both the importance and difficulty of this kind of long-term follow-up. It has taken Drs Orringer and Stirling 12 years to follow 76 patients for at least 5 years. The average age of the patients was 51 years, and they have at least a 25-year life expectancy with this benign disease. It has taken us more than 20 years to collect 100 patients followed for longer than 10 years. If I reflect on this, I find that I would hesitate to change an operation without a very clearly perceived need, because to do so means I'm certain I'll never live long enough to see the results in a meaningful long-term follow-up.

I have two questions for Dr Stirling. I assume the Collis-Nissen procedure is your operation of choice. Is it the sole operation used for conservative antireflux reconstruction? If you do use other repairs, in what circumstances are they used? And could you clarify your definition of paraesophageal hernia? To me it means a hernia in which the esophagogastric junction lies below the diaphragm. I assume with the high percentage of such patients in your report, that you are referring to a rolling hernia or a massive herniation with intrathoracic stomach and volvulus.

I very much appreciate the opportunity to review this manuscript and discuss the paper.

DR STIRLING: I thank Dr Pearson for his comments and acknowledge his extensive experience and excellent results in antireflux surgery.

In answer to his questions, we do use other operations besides the Collis-Nissen operation for antireflux procedures. Although we use the Collis-Nissen operation in the majority of our patients, we choose the Nissen fundoplication in patients who are thin, without hiatal hernias or with small hiatal hernias and minimal esophageal shortening, and without substantial esophagitis.

The vast majority of paraesophageal hiatal hernias in this series were type III hernias, which have an associated sliding component and usually some esophageal shortening.

At this meeting we have heard both Dr Grillo and Dr Cooper emphasize Dr Halsted's credo that the operating room should be the surgeon's laboratory. However, the traditional aim of esophageal operations has been a satisfied customer, hardly a quantifiable result. Objective follow-up and application of statistical methodology to patients undergoing antireflux operations add a new and more meaningful dimension and provide better justification either for continuing an approach or altering it to improve results.

REVIEW OF RECENT BOOKS

International Trends in General Thoracic Surgery. Volume 3. Benign Esophageal Disease
Edited by Tom R. DeMeester and Hugoe R. Matthews
St. Louis, C.V. Mosby, 1987
385 pp, illustrated

Reviewed by Kamal A. Mansour, MD

This is the third volume in the series *International Trends in General Thoracic Surgery*. The editors address the subject of esophageal reflux extensively and elaborately, with much detail, repetition, and discussions, and with an international flavor—a task they should be highly commended for. Accordingly, the book should have been entitled "Gastroesophageal Reflux Updated" or "Recent Advances in Gastroesophageal Reflux" rather than "Benign Esophageal Disease."

The function of the esophagus, the pathophysiology of gastroesophageal reflux, an update on esophageal pH monitoring, and the recent advances in esophageal manometry, endoscopy, ultrasonography, scintigraphy, and tests of duodenogastric function are very well detailed. The principles of surgical management, the advantages and disadvantages of different antireflux procedures, and the management of failed antireflux procedures are described. Even discussion of the controversial Angelchik prosthetic device is included. The pathophysiology of gastroesophageal reflux in children, clinical manifestations, diagnosis, and medical versus surgical therapy are discussed. The chapter on the controversial subject of Barrett's esophagus is complete and well referenced. The management of reflux strictures and caustic injuries, as well as the increasingly common drug-induced esophageal injuries, is clearly and refreshingly presented. The discussion of the controversial operation for achalasia and diffuse esophageal spasm and managing the failed Heller's operation is excellent. Finally, the section on pharyngeal dysphagia and proximal esophageal strictures is nicely outlined.

Admittedly, the subject of gastroesophageal reflux constitutes the most important benign esophageal problem, and should be discussed in a timely fashion as outlined in this excellent monograph. However, other benign esophageal problems such as congenital disorders (particularly esophageal atresia with tracheoesophageal fistula), traumatic and spontaneous rupture of the esophagus, foreign bodies in the esophagus, inflammatory disorders such as candidiasis and Crohn's disease, and benign tumors of the esophagus were totally ignored and should have been included.

I recommend this book very highly for those of us who are interested in in-depth study of gastroesophageal reflux, its complications, and its associated disorders, even if the title of the book is misleading.

Atlanta, Georgia

Closure of Chronic Postpneumonectomy Bronchopleural Fistula Using the Transsternal Transpericardial Approach

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Thirteen patients with postpneumonectomy bronchopleural fistula occurring 4 months to 10 years after the initial operation have been treated with a transsternal transpericardial approach after the associated empyema had been treated by either tube thoracostomy or open-window thoracostomy. In 10 patients, there were contraindications to using an ipsilateral transthoracic approach. In 10 of the 13 patients, the procedure was successful. Three fistulas recurred; two were quite small, one of them closing spontaneously within 6 months. There were no deaths or clinically significant morbidity related to the transsternal approach. We have found this technique to be most applicable in those patients in whom other procedures have failed to resolve the problem. The technique is relatively simple and safe.

(Ann Thorac Surg 1989;47:231–5)

With modern surgical techniques, a bronchopleural fistula after pneumonectomy should be rare, but these fistulas still complicate up to 5% of such procedures [1]. Fistulas occurring in the early postpneumonectomy period are best treated by immediate reoperation and reclosure, augmented by a protective patch of well-vascularized tissue. Fistulas occurring later (weeks to years postoperatively) are usually managed initially by tube drainage as most patients are seen with a fistula plus an empyema. Ultimately, both the fistula and the empyema must be dealt with.

Many methods have been used to close the chronic postpneumonectomy bronchial fistula. Open-window thoracostomy as described by Clagett and Geraci [2] deals with the associated empyema and can ultimately result in spontaneous closure of some of the smaller fistulas [3]. Nonsurgical maneuvers including repeated bronchoscopic cauterization of the fistula [4] or the application of fibrin glue [5] have been described as being somewhat successful. Direct surgical methods of managing this problem include repeat thoracotomy with reclosure of the bronchus using a vascularized patch (pericardium, muscle, or omentum) for reinforcement [6], large myovascular bundles to simultaneously close the fistula and cavity [7], or nearly total thoracoplasty. A contralateral right thoracotomy approach to the left main bronchus has also been successful in cases of chronic fistulas after left pneumonectomy [8].

In 1960, Padhi and Lynn [9] in Canada were among the first to document a transpericardial approach to close chronic postpneumonectomy fistula utilizing anterior thoracotomy with division of multiple costal cartilages. One year later, Abruzzini [10] in Italy described the transsternal transpericardial approach. This has been employed extensively in Russia by Perelman and Ambatiello [11] and Bogush and colleagues [12]. The technique was reintroduced in centers in North America in the 1980s [13, 14]. In the past 10 years, we have had 13 patients in whom the transsternal transpericardial approach was used for closure of chronic bronchopleural fistulas following pneumonectomy.

Material and Methods

In all patients, preoperative drainage of the postpneumonectomy space had been effected by tube thoracostomy or open-window thoracostomy, or both. To facilitate intraoperative ventilation in the presence of a bronchopleural cutaneous fistula, a variety of anesthesia techniques were used, including double-lumen tubes, long single tubes inserted into the remaining bronchus, an endobronchial blocker in the stump of the pneumonectomy, packing the open stump through the thoracostomy window, and high-frequency jet ventilation.

We use a full median sternotomy (Fig 1). After the mobilization and retraction of the superior vena cava and the aorta (Fig 2), the lower trachea above the pericardial reflection is mobilized; care is taken to avoid injury to the left recurrent nerve. The anterior pericardium is opened, and the pulmonary artery is either mobilized and retracted inferiorly or reamputated to effect better exposure. The posterior pericardium is then opened behind the pulmonary artery, thereby totally exposing the carina (Fig 3). A substantial shift of the mediastinum as a result of the pneumonectomy can make this exposure somewhat difficult, especially on the left.

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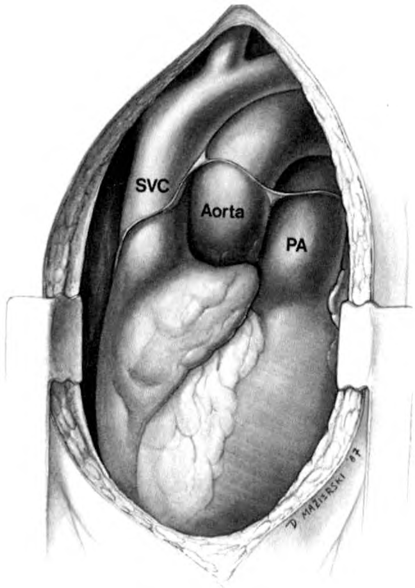

Fig 1. A full sternotomy incision has been made. The anterior pericardium has been opened, exposing the great vessels. (PA = *pulmonary artery;* SVC = *superior vena cava.)*

The affected bronchial stump is then dissected at the carina, isolated, and divided. This reamputated stump is closed using interrupted sutures or staples. The suture line is reinforced with vascularized pericardium. The distal stump is totally excised if possible (Fig 4). Alternatively, after the distal stump mucosa has been destroyed by cauterization (either at bronchoscopy before the procedure or at the surgical operation), the proximal end of this remaining stump is closed and left in situ.

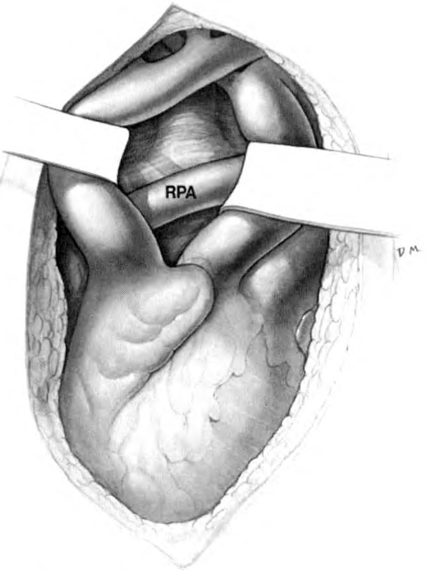

Fig 2. Retraction of the superior vena cava and aorta to each side exposes the right pulmonary artery (RPA) *and the posterior pericardium overlying the carina.*

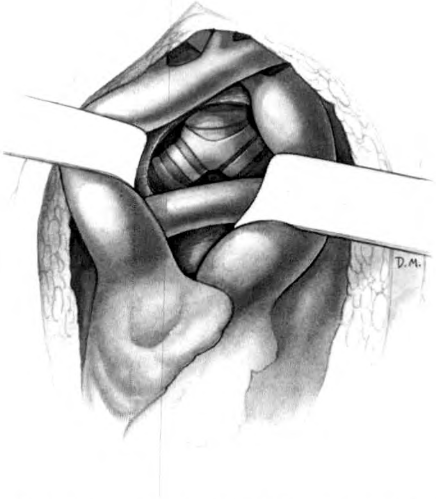

Fig 3. A wide incision of the posterior pericardium totally exposes both bronchi and the lower trachea.

Results

We reviewed the records of 13 patients (8 men, 5 women) who had chronic postpneumonectomy fistulas closed utilizing this technique during the years 1978 to 1987. Age ranged from 38 to 73 years. In 9 patients, pneumonectomy

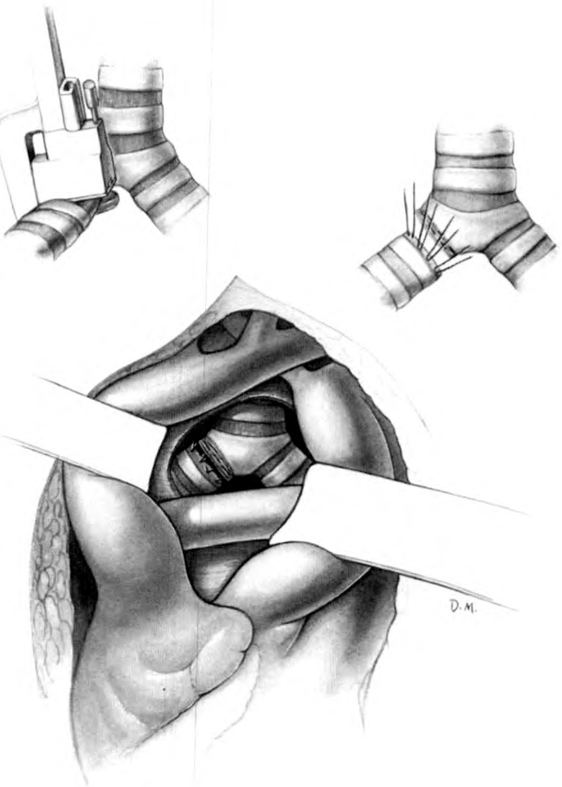

Fig 4. A chronic right fistula treated by division and reclosure of the proximal and distal stumps. Preferably, the distal stump should be excised, but this is not always possible.

was performed for carcinoma. The other 4 patients had irreversible inflammatory disease, including tuberculosis, bronchiectasis, bronchocentric granulomatosis, and necrotizing pneumonia. There were five left and eight right fistulas. The patients were seen 4 months to 10 years after development of the fistula.

In 10 patients, there were associated problems that did not allow a simple ipsilateral thoracotomy approach. The problems included previous attempted single or multiple closures by ipsilateral thoracotomy (3 patients), previous thoracoplasties with or without associated myovascular flaps that had failed (3 patients), persisting infection in a thick-walled postpneumonectomy space (3 patients), and associated tracheal stricture (1 patient). In 3 other patients, the transsternal approach was elected as the first closure attempt. There was no postoperative mortality or clinically significant morbidity.

In two instances, reamputation of the ipsilateral pulmonary artery stump allowed further exposure of the residual bronchial stump. In all patients except 1, the bronchial stump was redivided close to the carina and then sutured or stapled. In the 1 exception, the mobilized stump was stapled in continuity without transsection. In 9 patients, the reclosed bronchus was covered by a vascularized patch (pericardium or thymus, or both). In 1 patient with an associated low tracheal cuff stricture after intubation, a concomitant tracheal resection was performed, and pedicled omentum was used to cover the anastomosis.

A variety of techniques were used to handle the 12 residual distal stumps, including total excision (2 patients), cautery of the mucosa and proximal closure (6 patients), and cautery of the mucosa without proximal closure (4 patients).

In all patients, the empyema space was not closed initially but was handled by continued drainage through the thoracostomy window or tube.

In 10 patients, the bronchial closure healed primarily and has remained intact 18 months to 7.5 years later. Three patients have died in late follow-up.

There were three instances of failure of this technique. In the single patient in whom stapling was done without division of the bronchus, the fistula totally reopened within 1 week after closure as a result of failure of the staple line. The two other failures resulted in tiny recurrent fistulas, both in patients in whom multiple previous operations led to the closure of a difficult stump without closure of the distal remnant. One of these fistulas subsequently closed spontaneously within 6 months.

Comment

The technique of transsternal closure of bronchopleural fistulas has been well described by Abruzzini [10] and Perelman and Ambatiello [11]. In most cases, the associated empyema cavity will have been drained by tube or open-window thoracostomy before closure of the fistula. The selection of anesthesia technique depends on the situation at hand. We found a variety of techniques useful, including double-lumen tubes, a bronchial blocker to occlude the stump, a long endotracheal tube to ventilate the contralateral (usually left) mainstem bronchus, and high-frequency jet ventilation. In one instance, the fistula was occluded by packing through the thoracostomy window.

Although the right mainstem bronchus can be exposed extrapericardially with a transsternal approach, we have found that the best exposure is obtained by opening the anterior pericardium, retracting or reamputating the ipsilateral main pulmonary artery, and then opening up the posterior pericardium to expose the total carinal area. Once the affected bronchial stump has been isolated near the carina, division and reclosure by suture or staple is imperative. We and others [14] have experienced failures caused by stapling in continuity without division. This should be avoided. Once the proximal stump has been closed, we believe it important to attempt to reinforce the closure with adjacent vascularized pericardium, mobilized thymus, or omentum, which is easily obtained on a vascular pedicle from the upper abdomen through an extension of the median sternotomy. The omentum can be extremely valuable, especially in very difficult dissections or whenever the blood supply to the closure appears tenuous (eg, after irradiation).

If possible, the distal remnant stump should be totally excised to avoid mucus secretion in the empyema cavity. If this is not technically feasible, the mucosa should be obliterated either at the time of operation by cauterization or just before operation by electrocoagulation or laser cauterization through a bronchoscope. The proximal end of this stump should be closed whenever possible. Ultimately, the residual empyema cavity can be sterilized by the method of Clagett and Geraci [2] or closed by large myovascular flaps or thoracoplasty.

Although there are many approaches to facilitate closure of a chronic postpneumonectomy bronchopleural fistula, we have found the transsternal transpericardial approach relatively simple and effective. The single disadvantage of this method is that the residual empyema space is not dealt with at the same time, unlike myovascular transpositions or thoracoplasty. This technique is most useful when there are contraindications to performing an ipsilateral transthoracic approach. In some instances, with extreme shifts of the mediastinum, especially to the left after a left pneumonectomy, the anterior thoracotomy approach described by Padhi and Lynn [9], in which multiple costal cartilages are divided or excised, has theoretical advantages, allowing a more direct approach to the pericardium and left mainstem bronchus.

The technique of transsternal transpericardial resection of chronic postpneumonectomy bronchopleural fistulas should be placed in the armamentarium of all thoracic surgeons, and is most advantageous when a direct approach through the ipsilateral thoracotomy space is contraindicated or when previous attempts at closure have failed.

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DISCUSSION

DR PETER L. PAIROLERO (Rochester, MN): I thank Dr Ginsberg and his colleagues for calling to our attention yet another method to manage chronic bronchopleural fistula, which can occur after pneumonectomy. Although a rare complication, bronchopleural fistula in this situation can at times be life-threatening. It is important to note, however, that this is not a single complication but actually two, namely, bronchopleural fistula and postpneumonectomy empyema. Consequently, for these two complications to be successfully treated, not only must the fistula be closed but the pneumonectomy pleural space must also be ultimately obliterated and the chest wall eventually closed. Thus, closure of the fistula by any means is only partial treatment of this problem, and our colleagues from Toronto are among the first to point this out. Because the thrust of their presentation is an alternative method of closure of the fistula, I will make no further comments regarding management of the associated empyema other than to mention that open-window thoracostomy with frequent mechanical debridement by wet-to-dry dressing changes followed by secondary chest wall closure as described by Clagett some 25 years ago remains highly effective.

Transsternal closure of a bronchopleural fistula is not applicable to all patients. As Ginsberg and his colleagues clearly pointed out, bronchopleural fistula occurring in the immediate postoperative period is best treated not by the transsternal route, but by immediate reoperation through the original lateral thoracotomy with subsequent reclosure of the bronchial stump followed by reinforcement with well-vascularized tissue. In our practice, this has been intrathoracic transposition of extrathoracic skeletal muscles, such as the serratus anterior muscle.

What about patients in whom a fistula occurs weeks to years after pneumonectomy? Certainly, they are more difficult to manage. All too frequently, treatment in these patients is limited to management of the associated postpneumonectomy empyema, initially by pleural drainage, usually eventually open pleural drainage, and later by thoracoplasty, muscle transposition, or other pleural space–reducing maneuvers. This was the setting in 10 of the patients of Dr Ginsberg and associates. Certainly, direct dissection of the hilar structures through a lateral approach in a patient who has had multiple pleural space operations is at best tedious and at worst life-threatening because of massive hemorrhage, and I agree that persistent fistula in this clinical situation can be better managed with a transsternal approach.

Are there contraindications to transsternal closure? I have several questions for Dr Ginsberg. What about the patient who has had a prior cardiac operation? Can the transsternal route still provide adequate exposure safely? Also, how long does the stump have to be for this approach to be effective? What about the patient who has no stump whatsoever but rather has an open lateral carinal wall? Can the transsternal approach still be used?

Finally, what did happen to the empyema cavity in your patients? Did any patient eventually have the chest wall closed?

Again I congratulate the Toronto group for their alternative method of management of a very difficult problem.

DR P. KNAEPEN (Nieuwegein, the Netherlands): Dr Ginsberg and colleagues are to be congratulated for the outstanding results obtained in the treatment of this life-threatening complication after pneumonectomy.

At the St. Antonius Hospital, Nieuwegein, we have been performing this type of operation for almost 20 years, and it has become our procedure of choice in patients with large bronchopleural fistula. I suppose Dr Ginsberg would agree that we should restrict this major operation to this particular group of patients. Our overall results are less satisfactory than those of his group. Univariate analysis showed that the most important predictor of hospital mortality was recurrence of the bronchopleural fistula.

In 25 patients without recurrence of fistula, hospital mortality was 12%. However, once a bronchopleural fistula recurred, and this was the case in 7 patients, mortality was extremely high—57%.

The best way to prevent recurrences and the associated mortality is aggressive treatment of the empyema. In our initial experience with 17 patients, repeat thoracentesis or tube drainage was used, and the recurrence rate was very high—35%. Since 1982, when open-window thoracostomy has been routinely performed before the closure procedure (15 patients), the recurrence rate has dropped dramatically to 7%, and so has hospital mortality.

On the basis of this experience, we believe that transpericardial closure of bronchopleural fistula per se is not the final answer, but that open-window thoracostomy should be an integral part of the total treatment. How many times, Dr Ginsberg, have you used tube drainage alone, and was there any relation to the recurrences?

Finally, although we fully support your recommendations to avoid failures, we do not agree with your method of leaving the thoracostomy window open. It is a terrible burden for the patient, both physically and psychologically. Dr Ginsberg, could you explain to us why you do not close the window after successful closure of the bronchopleural fistula?

DR JAMES P. GEIGER (San Francisco, CA): I compliment the authors on their success with this procedure, but I wonder about the management of their failures. I also express some dismay at the length of the bronchial stump.

The opportunity to learn thoracoplasty and myoplasty techniques is rarely available to trainees today. This explains why some patients are advised that there is no suitable treatment. During 20 years of duty at Army referral centers, and subsequently in private practice, I have seen a variety of problems and associated fistulas. These include active tuberculosis, war wounds, postirradiation pneumonectomy, necrotizing pneumonia, and draining empyema after pneumonectomy and prior thoracoplasty for tuberculosis.

I have utilized a technique described by Dr John Grow of Denver (*Diseases of Chest*, Vol 12, 1946). This technique has been 100% successful in my large number of inherited cases.

The principles include drainage and local control of sepsis, special attention to nutrition, and restoration of positive nitrogen balance. Preserve all the muscle, excise all the rigid parietal scar, and suture a viable muscle pedicle flap over the fistula, followed by layer closure. Psychological support has been important in most patients.

DR GINSBERG: I thank all the discussants for their comments.

In answer to Dr Pairolero's questions, we have not had any patients who have undergone previous cardiac operations. This could create a very difficult situation, especially if the intrapericardial area is scarred. I wonder whether the anterolateral parasternal thoracotomy might be valuable in this instance, but it is one situation that we've not encountered. Dr Pairolero and all the other speakers did emphasize the necessity of adequate drainage of the empyema cavity as a very important and integral part of this management.

Dr Pairolero also asked about the minimum length of stump that we could close and what would happen if there was a lateral tracheal defect left after multiple previous operations. I think the transsternal approach would be the best approach for that very difficult problem. You can do a lateral patch. Omentum or some other patch reinforced by omentum would be very valuable when total closure of the stump cannot be done or there is a lateral opening in the trachea. I think this would be an indication for the transsternal approach.

What happened to the cavities that we did not treat primarily? Three patients died of carcinoma within 2 years and had no cavity treatment, and 3 patients were treated by either thoracoplasty alone, myoplasty plus thoracoplasty, or myoplasty alone. The other patients accepted the thoracostomy window and did not want another operation, and they are alive and well with the thoracostomy window.

Dr Knaepen mentioned that this was the procedure of choice for a long stump. I think this is the procedure of choice when the other attempts at closure have failed. Certainly if there is a long stump, one can dissect the bronchial stump and remove it, but this can be difficult. The high mortality he reported was, I'm sure, related to the fact that the empyema cavities were not adequately drained before elective closure of the bronchopleural fistula. We all agree that there has to be adequate drainage of the space. In only 3 of our patients was tube thoracostomy drainage used, and that was when the patient had had previous thoracoplasty with a very tiny space. Only a tube could be inserted; a window could not be created.

I thank Dr Geiger for reminding us of the value of myovascular bundles in the management of this disorder.

Clinical and Hemodynamic Results After Mitral Valve Replacement in Patients With Obstructive Hypertrophic Cardiomyopathy

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Mitral valve replacement has been performed in patients with obstructive hypertrophic cardiomyopathy if: (1) the interventricular septum is smaller than 18 mm in the region of usual resection; (2) atypical septal morphology is encountered; (3) a previous left ventricular myomectomy has been performed but residual major obstruction and symptoms persist; or (4) intrinsic mitral valve disease exists. Since 1983, mitral valve replacement has been performed in 58 patients with obstructive HCM only. Thirty-three female patients (mean age, 47.9 years) and 25 men (mean age, 45.7 years) met criteria 1 through 3 for mitral valve replacement. Patients with intrinsic mitral valve disease (criterion 4) were omitted from this study. All patients were in New York Heart Association functional class III or IV and had failed optimal medical therapy. Low-profile mechanical prostheses and bioprostheses were implanted, and the early mortality (<30 days or in the hospital) was 8.6% (5/58). Six patients (11.3%) died late, 3 suddenly of probable arrhythmia, 2 of respiratory failure, and 1 of an anticoagulant-related complication. After mitral valve replacement, 40 (83%) of 48 patients surviving operation and returning for evaluation were in functional class I or II, whereas 8 patients were in functional class III. Hemodynamic data obtained 6 months postoperatively showed that pulmonary artery wedge pressure was normal (13.7 ± 4 mm Hg [± standard deviation]), left ventricular end-diastolic pressure had decreased (10.9 ± 3.4 mm Hg), cardiac index was maintained (2.6 ± 0.6 L/min/m^2), and resting and provoked gradients were unremarkable. Mean follow-up was 24.2 months, actuarial survival was 86% at 3 years, and survival free from thromboembolism, anticoagulant-related complication, reoperation, and congestive heart failure for the same interval was 68%. Complications such as ventricular septal defect and complete heart block are avoided in patients undergoing mitral valve replacement, but device-related and cardiac-related complications can add to the morbidity and mortality in these patients in the long term.

(Ann Thorac Surg 1989;47:236–46)

The introduction of echocardiography in the early 1970s provided a noninvasive diagnostic tool for detecting nonobstructive and obstructive hypertrophic cardiomyopathy (HCM), and elucidated the mechanism of obstruction in this disease [1, 2]. In the 1980s, it has provided intraoperative information used in determining the choice of operation to be performed. Treatment of symptomatic patients with HCM over the past 30 years has included medical therapy using β-blockers in the 1970s and calcium antagonists more recently.

Operative intervention in patients with HCM was intended to relieve the left ventricular outflow tract (LVOT) obstruction, and has been reserved for those patients failing optimal medical therapy. Morrow [3] pioneered and perfected the left ventricular (LV) myomectomy and performed this operation in 350 patients [4, 5]. He believed strongly that the intrinsically normal mitral valve (MV) should never be removed and replaced with a prosthesis in the treatment of obstructive HCM. Other operative approaches for relief of LVOT obstruction by removal of septal muscle include the LV apical approach [6, 7] and the right-sided septal resection [8, 9]. As the mechanism of obstruction in HCM is systolic anterior motion of the anterior MV leaflet, which contacts the septum, Cooley and colleagues [10, 11] suggested mitral valve replacement (MVR) to correct the LVOT gradient.

This report is the first from the Surgery Branch of the National Heart, Lung, and Blood Institute concerning 58 patients having obstructive HCM only who underwent MVR based on specific intraoperative M-mode and two-dimensional echocardiographic criteria and who were not good candidates for LV myomectomy in this clinic. Fifty-three patients survived MVR, 48 of whom were studied intensively approximately 6 months postoperatively. These studies included cardiac catheterization to determine the efficacy of MVR in the operative treatment of obstructive HCM.

Material and Methods

Mitral valve replacement was performed in 58 patients having obstructive HCM only; there was no concomitant coronary artery disease or other cardiac lesions. All pa-

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Table 1. Criteria for Mitral Valve Replacement in Patients With Obstructive Hypertrophic Cardiomyopathy

Criterion	No. of Patients
Interventricular septum <18 mm in usual region of resection	29
Atypical septal morphology	14
Previous left ventricular myomectomy with persistent obstruction and symptoms	15
Organic mitral valve disease and HCM (excluded for this study)	(4)
Total	58

HCM = hypertrophic cardiomyopathy.

Table 2. Prosthetic Mitral Valves Used in Patients With Obstructive Hypertrophic Cardiomyopathy

	Size (mm)					
Valve	23	25	27	29	31	Total
Björk-Shiley (model MBRP)	19	20	7	1	0	47
St. Jude (model 101M)	2	1	0	0	1	4
Hancock bioprosthesis (models 342, 342R)	0	4	3	0	0	7

tients were admitted to the Cardiology Branch on HCM protocols and underwent the following: collection of history; physical examinations; laboratory, two-dimensional, and M-mode echocardiography; electrocardiography; radionuclide angiography; exercise tolerance testing; and cardiac catheterization. Catheterization studies were performed after all cardiac medications were discontinued, and included right and left heart pressure measurements, evaluation of resting and provoked gradients, cardiac output, angiographic assessment of LV function and MV and aortic valve regurgitation, and coronary arteriograms. Patients having a resting gradient higher than 100 mm Hg did not undergo provocative tests. Electrophysiological studies were performed in select patients whose history included ventricular fibrillation or major ventricular tachycardia.

There were 33 female patients whose mean age was 47.9 years (range, 16 to 78 years) and 25 men with a mean age of 45.7 years (range, 25 to 63 years). All patients referred for operation were in New York Heart Association (NYHA) functional class III or IV, and all had failed optimal medical therapy including verapamil hydrochloride, β-blockers, and diuretics. Amiodarone therapy was discontinued 3 to 6 months before operation if possible.

Mitral valve replacement was usually performed through a median sternotomy. Five patients with a previous LV myomectomy, increased anteroposterior chest diameter, normal left atrial dimensions, or marked hypertrophy of the left ventricle and interventricular septum (IVS) had a right anterolateral or left posterolateral thoracotomy. Before institution of cardiopulmonary bypass, long-axis and short-axis two-dimensional echocardiograms were obtained using a sterile transducer and an Irex Meridian echocardiographic console (Johnson and Johnson, King of Prussia, PA) to determine the thickness of the IVS, distribution of septal hypertrophy, and the contact point of MV systolic anterior motion below the aortic annulus. The short-axis view was helpful in assessing the location and extent of hypertrophy of the IVS relative to the aortic annulus, which constituted the "operative window" if an LV myomectomy was to be performed. Table 1 shows the current criteria for MVR in patients with HCM, and the distribution of the 58 patients.

Myocardial preservation included total body hypothermia to 26°C, NIH cold oxygenated crystalloid cardioplegia, and iced saline slush. Cardioplegia administration was repeated every 20 to 25 minutes. Mitral valve replacement was performed using standard operative methods. The anterior and posterior MV leaflets were completely excised regardless of the type of prosthetic valve used.

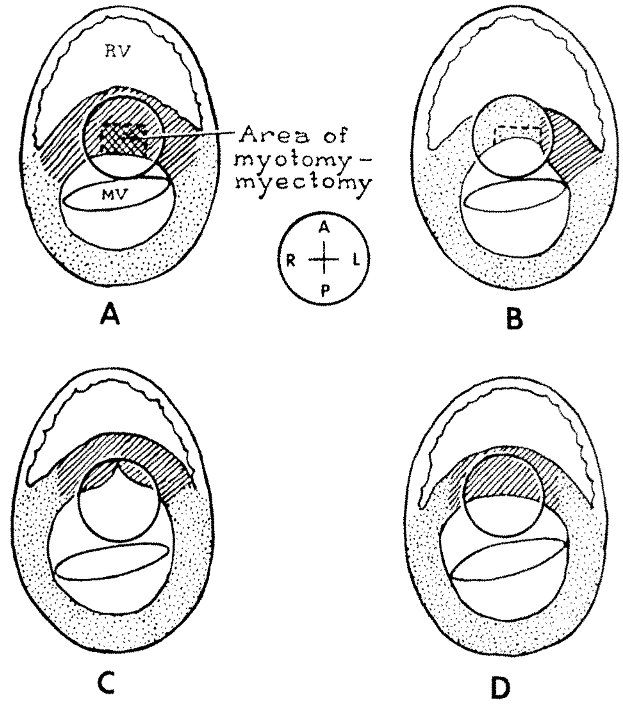

Fig 1. Illustrations of short-axis echocardiograms showing variation in thickness of interventricular septum and distribution of hypertrophy in relation to aortic annulus, which constitutes the "operative window." The aortic annulus is represented as a circle overlying the septa. A. Marked homogeneous hypertrophy of anterior IVS permits left ventricular myomectomy. B. Hypertrophy of IVS can be displaced lateral to aortic annulus, thereby not permitting LV myomectomy in anterior septum. C. Prominent notch in anterior IVS with insufficient septum exposed for effective LV myomectomy. D. Relatively thin (<18 mm) anterior IVS compared with (A). Examples (B), (C), and (D) constitute indications for mitral valve (MV) replacement. (A = anterior; L = (patient's) left; P = posterior; R = right; RV = right ventricle.)

Table 3. Causes and Potential Preoperative Risk Factors of Early Death After Mitral Valve Replacement for Obstructive Hypertrophic Cardiomyopathy

Patient No.	Sex	Age	Cause(s)	Risk Factor(s)
1	M	29	Hepatorenal failure (18 days postoperative)	Amiodarone therapy
2	F	39	Mechanical prosthetic valve failure (Björk-Shiley) (1 day postoperative)	None
3	F	45	Hepatorenal failure, low cardiac output (6 days postoperative)	Amiodarone therapy
4	F	56	Sepsis (15 days postoperative)	Functional class IV, low cardiac output, sepsis, COPD
5	F	58	Ventricular fibrillation secondary to pacing after placement of RV wire for digitalis toxicity (15 days postoperative)	Functional class IV, pulmonary artery hypertension, paroxysmal atrial fibrillation, cardiac cachexia

COPD = chronic obstructive pulmonary disease; RV = right ventricular.

Pledget-reinforced horizontal mattress sutures of 2-0 Tevdek (Deknatel, Floral Park, NJ) were used because the MV remnant and annulus were usually normal. Prosthetic valves and sizes used are shown in Table 2. The left atrial appendage was obliterated in patients with chronic atrial fibrillation.

During rewarming, early maneuvers to remove air were used because many hearts developed a spontaneous rhythm and frequently overrode the perfusion pressure in the first few beats. Atrial and ventricular temporary pacing wires were used in all, and atrioventricular sequential pacing was instituted when necessary. An intraoperative echocardiogram was not routinely performed after MVR unless there was difficulty in weaning the patient from cardiopulmonary bypass, in which case it was used to determine possible prosthetic valve dysfunction.

Epicardial sensing electrodes and automatic internal cardiac defibrillator (AICD; Cardiac Pacemakers, Inc, St. Paul, MN) patches were implanted in patients demonstrated to have ventricular arrhythmias by electrophysiological study who might require an AICD in the future. These leads were tested, capped, and implanted in the left upper quadrant, but the AICD was not implanted at the time of MVR.

Postoperative care included, when indicated, inotropic and afterload-reducing drugs, digitalis, and use of the intraaortic balloon pump. Patients in whom a mechanical prosthesis was implanted were placed on a regimen of warfarin sodium, and the prothrombin time was maintained in the range of 20 to 25 seconds. Individuals receiving a bioprosthesis ($n = 7$) were not routinely anticoagulated unless they were in chronic atrial fibrillation ($n = 1$). Antiarrhythmic drugs were used for management of ventricular and supraventricular arrhythmias until further evaluation after MVR was performed. Some patients were continued on a regimen of β-blockers or verapamil, or both, postoperatively for control of heart rate or of persistent symptoms.

Postoperative follow-up usually included two-dimensional, M-mode, continuous, and color-encoded Doppler echocardiography, radionuclide angiography, exercise tolerance testing, and cardiac catheterization, the last being performed after all cardiac medications except antiarrhythmic agents were discontinued for comparison with

Table 4. Causes and Risk Factors of Late Death in Patients With Obstructive Hypertrophic Cardiomyopathy

Patient No.	Sex	Age	Cause(s)	Risk Factor(s)
1	M	53	Respiratory failure, CHF (51 mo postoperative)	Previous LV myomectomy 21 mo before MVR, leak after MVR, obesity, functional class IV, COPD
2	F	68	Anticoagulant-related complication: subdural hematoma (21 mo postoperative)	Atrial fibrillation
3	M	60	Respiratory failure, CHF (12 mo postoperative)	Previous LV myotomy; COPD, obesity
4	F	25	Sudden: possible arrhythmia (18 mo postoperative)	Two previous myomectomies, ventricular arrhythmia
5	F	39	Sudden: possible arrhythmia or myocardial infarction (24 mo postoperative)	Functional class IV
6	F	67	Sudden: possible arrhythmia (8 mo postoperative)	CHF

CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; HCM = hypertrophic cardiomyopathy; LV = left ventricular; MVR = mitral valve replacement.

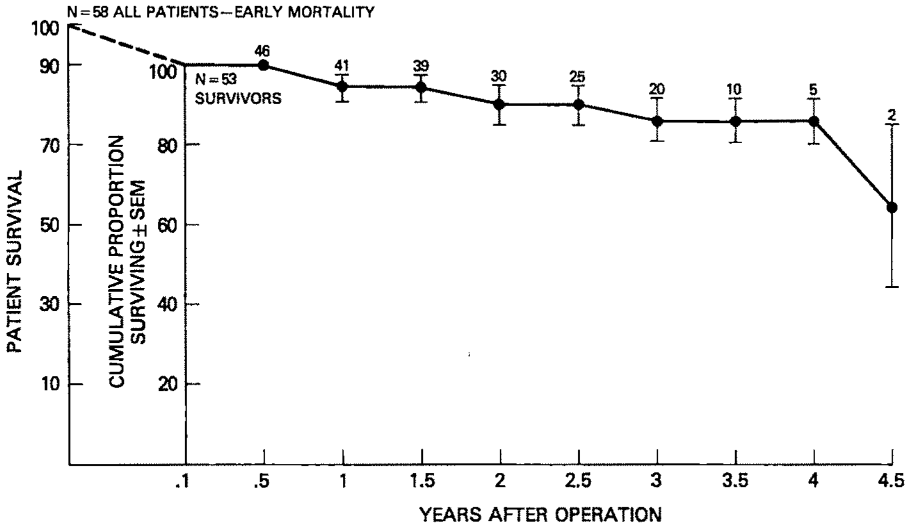

Fig 2. Actuarial probability of survival after mitral valve replacement for obstructive hypertrophic cardiomyopathy. Operative mortality (<30 days) indicated by broken line. (SEM = standard error of the mean.)

preoperative values. Patients were followed thereafter in the outpatient clinic on an annual basis.

Life-table estimates of patient survival and survival free from device-related or cardiac-related events were calculated by the actuarial methods of Cutler and Ederer [12] and Kaplan and Meier [13], and the probability estimates were expressed as the standard error of the mean (BMDP Statistical Software, University of California, Los Angeles, CA).

Results

Fifty-eight patients with obstructive HCM only by current criteria shown in Figure 1 underwent MVR. Five (8.6%) died in the early (<30 days or during hospitalization) postoperative period. The causes of early death and potential preoperative related risk factors are shown in Table 3. The 5 early deaths were associated with multiorgan failure, previous amiodarone therapy, stuck disc, an emergency, and a postoperative event in the electrophysiological laboratory. Late death occurred in 6 (11.3%) of the 53 survivors at a mean of 22.3 months after operation (range, 8 to 51 months). Causes of late death and potential preoperative risk factors are shown in Table 4. There were two respiratory failures, three sudden deaths, and one subdural hematoma. Actuarial survival of patients undergoing MVR for obstructive HCM is shown in Figure 2.

The preoperative and postoperative NYHA functional class is shown for 53 patients undergoing MVR (Fig 3). Forty-eight patients who survived operation have returned for postoperative evaluation; 83% are in functional class I or II. Eight (17%) patients are in functional class III, 3 of whom were in class IV preoperatively.

Hemodynamic studies were performed approximately 6 months after MVR. At the time of the studies, the patients were not taking any cardiac medications. The results are shown in Figures 4 and 5.

Analysis of preoperative and postoperative rhythm status of the 48 survivors is shown in Table 5. Seven pacemakers have been implanted, two preoperatively for sinus node dysfunction and high-grade distal heart block. Five pacemakers were implanted in the postoperative period for symptomatic Mobitz type II heart block (n = 3), tachy-bradycardia syndrome (n = 1), and junctional bradycardia with asystole (n = 1). Approximately 80% of patients are in normal sinus rhythm, and 6% are in atrial fibrillation.

Syncope has occurred in the late postoperative course in 3 patients and resulted in the death of 1. Postoperative catheterization had shown no clinically significant gradient at rest or on provocation in 2; the patient who died had not been studied. A fourth patient who had a history of ventricular fibrillation preoperatively had inducible ventricular tachycardia at the time of a postoperative electrophysiological study.

Valve-related or cardiac-related complications (reoperation, thromboembolism/amaurosis fugax, anticoagulant-related complications, and congestive heart failure [CHF]) are noted in Table 6. Probability of survival free from these complications is shown in Figure 6.

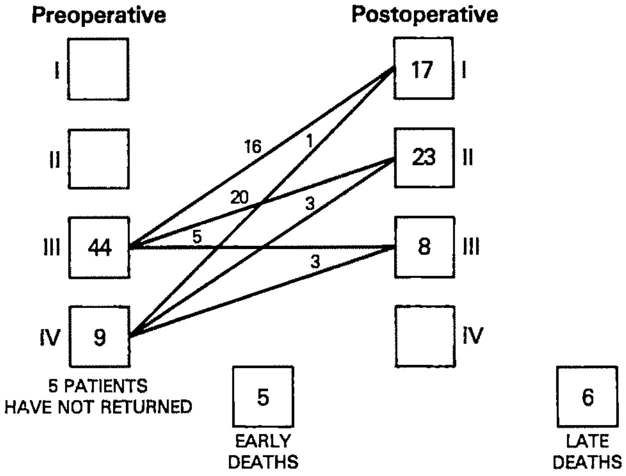

Fig 3. Preoperative and postoperative New York Heart Association functional class after mitral valve replacement for obstructive hypertrophic cardiomyopathy. Early (n = 5) and late (n = 6) deaths are noted.

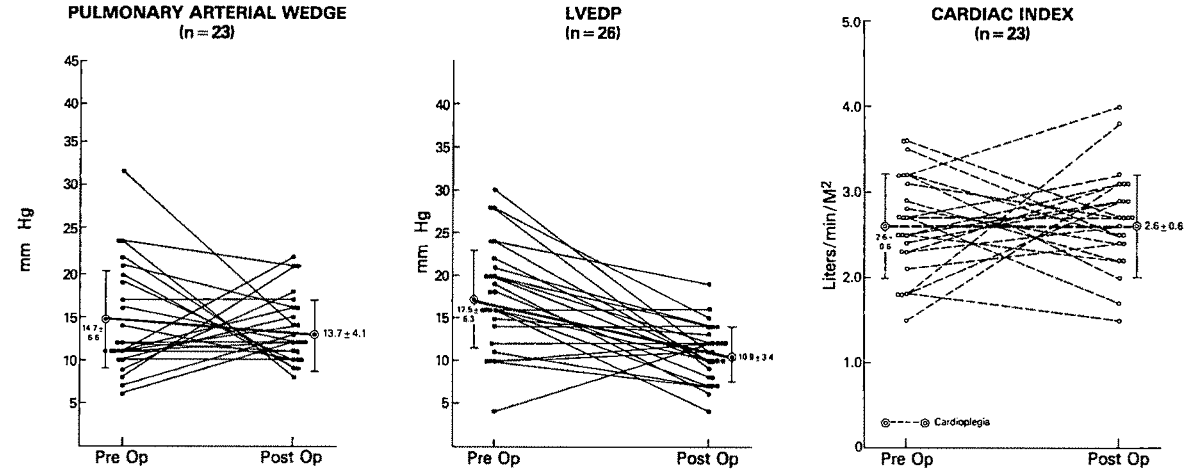

Fig 4. Preoperative and postoperative hemodynamic assessment of pulmonary artery wedge pressure, left ventricular end-diastolic pressure (LVEDP), and cardiac index after mitral valve replacement for obstructive hypertrophic cardiomyopathy. Values are expressed as the mean ± the standard deviation of the mean.

Reoperations, three cardiac and one vascular, were performed in 4 patients. Cardiac operations included replacement of thrombosed mechanical prostheses in 2 patients. One of them required two replacements at 34 and 41 months after the initial MVR, and the other underwent repeat MVR at 49 months. Both patients were on a regimen of warfarin, and their prothrombin times were in the therapeutic range at the time of thrombosis. One patient underwent repair of a paravalvular leak 8 months after MVR and survived the operation, but subsequently died of respiratory failure 51 months after MVR. The fourth patient, who had an intrinsic arteritis in

Fig 5. Preoperative and postoperative hemodynamic assessment of resting and provocable gradients after mitral valve replacement for obstructive hypertrophic cardiomyopathy. Post only *includes patients not undergoing maneuvers that would cause the gradient to rise preoperatively because of resting gradient greater than 100 mm Hg. Values are expressed as the mean ± the standard deviation of the mean.*

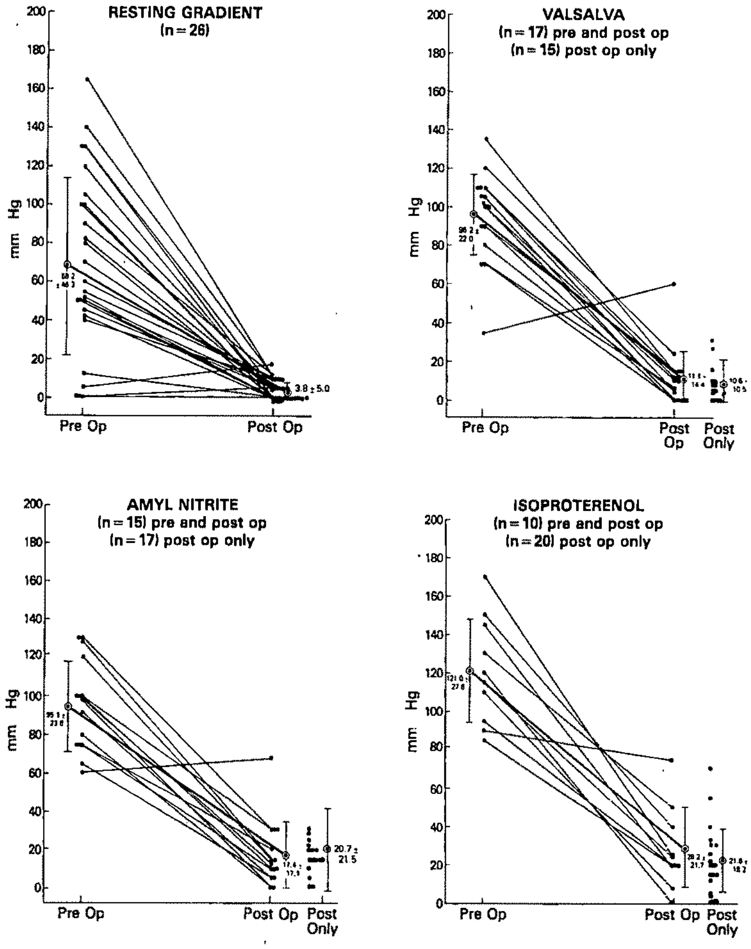

Table 5. Preoperative and Postoperative Rhythm Status in 48 Patients[a]

Rhythm	Preoperative	Postoperative
Normal sinus	41 (85.4)	38 (79.2)
Atrial fibrillation	5 (10.4)	3 (6.3)
Paced	2 (4.2)	7 (14.6)

[a] Numbers in parentheses are percentages.

addition to HCM and had been on long-term steroid therapy, required repair of a dissecting descending thoracic aortic aneurysm secondary to the aortic cannulation site.

Thromboembolism occurred in 3 patients and a single episode of amaurosis fugax in 2. A severe cerebrovascular accident occurred in a 42-year-old man 10 months after MVR with a Björk-Shiley prosthesis when warfarin therapy was discontinued for cardiac catheterization. He has no major motor or sensory defects, but continues to have expressive aphasia. Two patients underwent MVR with Hancock bioprostheses and were not on a regimen of warfarin therapy. One patient had a mild cerebrovascular accident 1 month postoperatively and is without sequelae, and the second had an embolus to an arm 1.5 months after MVR. All 3 patients were in normal sinus rhythm at the time of the event. The two episodes of amaurosis fugax occurred in patients with a Björk-Shiley prosthesis while they were on a warfarin regimen. Both patients were treated with dipyridamole and have had no recurrent events.

Anticoagulant-related complications occurred in 2 patients with a Björk-Shiley prosthesis. A 68-year-old woman sustained a fatal subdural hematoma 21 months after MVR, and a 30-year-old man required hospitalization and transfusion after a gastrointestinal hemorrhage. The prothrombin times could not be determined for these patients at the time of the event.

Two patients have had multiple episodes of CHF postoperatively; both had been in CHF preoperatively. A 25-year-old woman who had undergone two previous LV myomectomies, the first when she was 7 years of age, continued to have CHF after MVR and died suddenly, presumably of an arrhythmia. The second patient, a 40-year-old woman with long-standing systemic hypertension, has required several hospital admissions for CHF with no evidence of LVOT obstruction or prosthetic valve dysfunction.

Table 6. Valve-Related and Cardiac-Related Complications After Mitral Valve Replacement for Obstructive Hypertrophic Cardiomyopathy[a]

Complication	No. of Patients	Deaths
Reoperation	4 (7.5)	0
Thromboembolism/amaurosis fugax	5 (9.4)	0
Anticoagulant related	2 (3.8)	1
Congestive heart failure	2 (3.8)	1

[a] Numbers in parentheses are percentages.

HCM = hypertrophic cardiomyopathy; MVR = mitral valve disease.

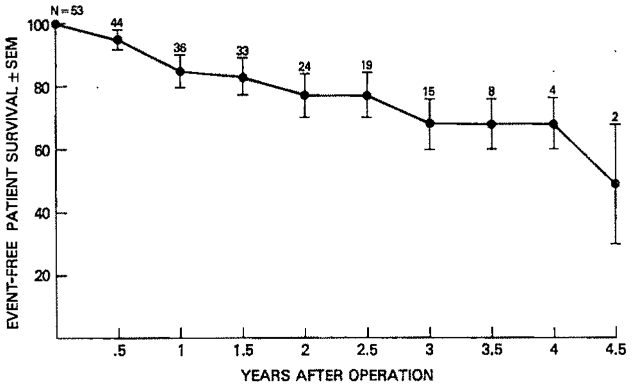

Fig 6. Actuarial probability of survival free from thromboembolism, anticoagulant-related complication, reoperation, and congestive heart failure after mitral valve replacement for obstructive hypertrophic cardiomyopathy. (SEM = standard error of the mean.)

Comment

Patients with obstructive HCM can experience symptoms of dyspnea, fatigue, chest pain, CHF, presyncope, and syncope. These symptoms can be attributed to the presence of dynamic LVOT obstruction [14], decreased ventricular compliance [15, 16], ischemia secondary to small vessel disease [17], mitral regurgitation [18], and atrial and ventricular arrhythmias [19]. The complex pathophysiology of HCM warrants an analysis of patients with this condition only so that symptomatic improvement, or lack thereof, after operative treatment is not compounded by the presence of coexisting valvular lesions or ischemia. This study includes 58 consecutive patients having obstructive HCM only who underwent MVR for relief of the LVOT gradient.

Operative intervention by either LV myomectomy or MVR will consistently and predictably relieve or reduce the dynamic obstruction [20, 21], but each procedure has associated short-term and long-term risks dependent on the morphology of the IVS or the device implanted. Iatrogenic ventricular septal defect, cardiac perforation, and complete heart block are known immediate risks identified with LV myomectomy, whereas MVR has more long-term device-related complications such as thromboembolism, complications resulting from anticoagulation, prosthetic valve dysfunction, or infection. Congestive heart failure can occur after LV myomectomy or MVR secondary to decreased ventricular compliance, ischemia, or the onset of atrial fibrillation, but can also be related to intrinsic prosthetic valve stenosis or regurgitation. Septal thickness and morphology can vary considerably in HCM, and therefore it was believed that criteria should be developed, based on intraoperative echocardiographic data, as to when MVR should be the procedure of choice.

Intraoperative echocardiography has been routinely performed since 1982, and the criteria that evolved for indications for MVR are shown in Table 1. It is believed that patients having relatively thin septa (<18 mm) will be at greater risk for iatrogenic ventricular septal defect or will have incomplete relief of LVOT obstruction if only a limited LV myomectomy can be performed. Atypical septal morphology illustrated in Figure 1 shows the hypertrophy to be displaced lateral to the aortic annulus (Fig 1B) and the presence of a prominent notch in the septum with insufficient muscle visible for LV myomectomy (Fig 1C). Forty-three patients (74%) had MVR as the primary operation for obstructive HCM based on atypical septal morphology or a septum measuring less than 18 mm. The remaining 26% (n = 15) of patients underwent MVR as a second operation; they had persistent NYHA functional class III symptoms and demonstrated clinically significant obstruction after LV myomectomy. If a patient has had an inadequate LV myomectomy and sufficient IVS remains by intraoperative echocardiography, a repeat LV myomectomy is performed.

Demonstration in the catheterization laboratory of systemic pulmonary artery hypertension or severe mitral regurgitation (3 to 4+) did not constitute an indication for MVR in patients having HCM. The creation of an adequate LVOT by myomectomy will reduce or abolish systolic anterior motion of the anterior MV leaflet and allow coaptation to the posterior MV leaflet during systole, thus reducing the mitral regurgitation.

Valve choice and operative techniques must take into consideration the unusual features of obstructive HCM. The markedly hypertrophied septum, and in some instances the LV free wall, result in a hypercontractile left ventricle and a small to normal-sized MV annulus. This highly contractile left ventricle can exert more force on the MV annulus during systole, which could distort the mitral prosthesis and result in dysfunction, especially if a larger-sized prosthesis is implanted. The Björk-Shiley prosthesis (model MBRP) was chosen because of its proven in vitro strength characteristics, long-term clinical durability, and excellent hemodynamic function in the small sizes (23 to 27 mm). However, because it is no longer manufactured in the United States, the St. Jude valve (model 101M) is being used more frequently. The Hancock bioprosthesis (models 342 and 342R) is used in patients who have contraindications to anticoagulation with warfarin. The use of smaller prostheses has not resulted in elevated pulmonary artery wedge pressures (see Fig 4) or major MV gradients at rest, and no patient has required reoperation for prosthetic valve stenosis. Considering the small dimensions of the LVOT during systole, the anterior MV leaflet is not left in situ, for systolic anterior motion can still occur, thereby causing persistent major LVOT obstruction. The posterior MV leaflet can be left, but probably is not necessary considering the hypercontractile characteristic of these hearts.

The Björk-Shiley prosthesis was oriented with its major orifice directed toward the LV free wall, and the St. Jude valve was placed with its leaflets in the same orientation as the native MV. The Hancock bioprosthesis is oriented so that the widest intrastrut distance is beneath the LVOT; therefore, if the two superior struts should contact the IVS, a channel remains for the outflow of blood. This can usually be achieved by placing the green marker suture on the sewing ring at the 2-o'clock position of the native MV annulus.

Mitral valve exposure through a median sternotomy is sometimes difficult because of the often normal size of the left atrium and the somewhat more anteroposterior orientation of the MV annulus secondary to marked hypertrophy of the IVS. A transatrial approach has been useful in such patients, as has approaching the MV by a right anterolateral or left posterolateral thoracotomy. Patients who have had a previous myomectomy and have marked hypertrophy of the IVS present the greatest exposure problem, and those with a thin IVS, the least.

Because of the extreme muscle mass associated with HCM, myocardial preservation included total body hypothermia to 26°C, NIH oxygenated crystalloid cardioplegia, and topical iced saline slush. Satisfactory myocardial protection was accomplished as demonstrated by the hemodynamic findings of preservation of the preoperative cardiac index at 2.6 ± 0.6 L/min/m^2 and the decreased LV end-diastolic pressure from 17.5 ± 6.3 mm Hg preoperatively to 10.9 ± 3.4 mm Hg after MVR.

Five patients (8.6%) died in the early postoperative period, 4 of whom had potential preoperative risk factors. Two patients who had received amiodarone therapy preoperatively died in the early postoperative period (6 and 18 days) of hepatorenal failure (1 patient) and low cardiac output and hepatorenal failure (1 patient). These 2 patients, a 29-year-old man and a 45-year-old woman, had serum glutamic-pyruvic transaminase and serum glutamic-oxaloacetic transaminase levels of 11,000 and 23,000 IU and 2,000 and 5,000 IU, respectively, within 48 hours after operation. Acute tubular necrosis requiring dialysis developed in both patients. Massive rhabdomyolysis was apparent in both as demonstrated by marked elevation of creatine kinase, which was predominantly MM band on fractionation. Neither patient had a prolonged period of hypoperfusion, hypotension, or hyperthermia during operation. We [22] believe that preoperative amiodarone therapy may be associated with increased mortality and morbidity in proportion to the total dose received in patients undergoing cardiac operations, and recommend the drug be discontinued 3 to 6 months before elective operation.

Two patients in NYHA functional class IV had multiple potential risk factors preoperatively (see Table 3), and operation was considered high risk but the only remaining option. A 56-year-old woman was receiving intravenous administration of Neo-Synephrine (phenylephrine hydrochloride) to treat low cardiac output secondary to severe obstruction, and was clinically septic with negative blood cultures when she was taken urgently to the operating room. She died 15 days postoperatively of sepsis and persistent low cardiac output. The second patient had systemic pulmonary artery hypertension, mitral regurgitation, and paroxysmal atrial fibrillation. Postoperatively she required ventilatory support for three days. She then slowly improved until a junctional bradycardia developed secondary to digoxin toxicity 15 days after MVR. She was taken to the electrophysiological laboratory for placement of a temporary pacing wire; there ventricular fibrillation developed, and she could not be resuscitated.

One valve-related death occurred in a 39-year-old woman who died on the first postoperative day of prosthetic valve malfunction. It was demonstrated by auscultation and arterial pressure measurements and confirmed by fluoroscopy that the disc of the Björk-Shiley prosthesis was intermittently sticking. The patient sustained two cardiac arrests; she was resuscitated after the first by a precordial thump, which freed the stuck disc. The second arrest was associated with deterioration of ventricular function, which precluded reoperation. At autopsy, no intrinsic cause such as thrombus, residual valve remnant, or long suture tail was identified.

Fifty-three patients survived MVR, and 48 have been evaluated approximately 6 months postoperatively. Hemodynamic evaluation revealed that the pulmonary artery wedge pressure had decreased from 14.7 ± 6.6 mm Hg to 13.7 ± 4.1 mm Hg after MVR using the smaller-sized prostheses (see Fig 4). Consistent and predictable relief of rest and provocable LVOT obstruction was demonstrated after valve replacement in patients with obstructive HCM (see Fig 5). Patients having rest obstructions greater than 100 mm Hg preoperatively did not undergo provocation because of the excessive LV systolic pressures that would be generated. These patients are noted as "postop only"; their obstructions probably represent the most severe, and the patients show excellent relief of provocable gradient. Provocation in this group by the Valsalva maneuver, amyl nitrite, and isoproterenol hydrochloride produced gradients of 10.6 ± 10.5, 20.7 ± 21.5, and 21.6 ± 18.2 mm Hg, respectively. The gradient at rest was essentially abolished, decreasing from 68.2 ± 46.3 to 3.8 ± 5.0 mm Hg after MVR. Mitral regurgitation, other than intrinsic transprosthetic regurgitation, which can be 1 to 2+ depending on the mechanical prosthesis, was corrected unless a paravalvular leak occurred (n = 2).

The relief of LVOT obstruction and reduction of LV systolic pressures is associated with symptomatic improvement as shown in Figure 3. It will be important to determine whether the symptomatic improvement at 6 months of 83% of patients to NYHA functional class I or II status will be maintained as has been demonstrated in the patients having LV myomectomy, 70% of whom reported functional improvement during an average follow-up of 5 years. This improvement after LV myomectomy occurred in the elderly population as well [23, 24], and the subjective relief of symptoms has been correlated with an objective increase in exercise capacity [25, 26] and threshold for pacing-induced angina [27, 28]. Patients having MVR for obstructive HCM are being studied in these protocols.

Actuarial survival after MVR at a mean follow-up of 24 months is 90% (n = 30) and at 3 years, 86% (n = 20). There have been 6 late deaths (11%) at a mean of 22.3 months (range, 8 to 51 months). Three patients who died late had previously undergone myomectomy, 1 of them twice, and had persistent NYHA functional class III or IV symptoms before MVR. After operation, 2 of these patients who had chronic obstructive pulmonary disease died of respiratory failure at 12 and 51 months after multiple hospitalizations. One of these patients required repair of a paravalvular leak 8 months postoperatively and did not have residual mitral regurgitation to account for the persistent respiratory failure. The third patient had undergone LV myomectomy at age 7 years, which was repeated at age 21 years, and MVR at age 23. She also was known to have ventricular tachycardia. This patient died suddenly at home, presumably of an arrhythmia. Two additional patients died suddenly at 8 and 24 months after MVR; the cause was most likely an arrhythmia. Arrhythmias appear to be a major cause of late death, and the increasing use of AICDs in patients identified by electrophysiological study to have major ventricular arrhythmias may increase survival among these individuals. The sixth patient died 21 months after MVR of a valve-related complication, a fatal subdural hematoma secondary to a complication of anticoagulation. Thus, of the 6 late deaths, only 1 appears to be valve related and the remainder were due to respiratory failure and arrhythmias.

As noted, complications related to implantation of a prosthetic device included reoperation (7.5%), thromboembolism (5.7%), anticoagulant-related complications (3.8%), and cardiac-associated CHF (3.8%). As these complications are cumulative after MVR, longer-term actuarial survival free from these events will be necessary to determine overall efficacy of MVR for obstructive HCM. Probability of survival free from thromboembolism, anticoagulant-related complications, reoperation, and CHF is 68% at 3 years.

Conclusion

Intraoperative echocardiography has been useful in defining variations in thickness and morphology of the IVS, which has resulted in the development of criteria for MVR for patients with obstructive HCM. Excellent hemodynamic results after MVR have been demonstrated in patients having an IVS smaller than 18 mm, atypical septal morphology, and incomplete relief of obstruction after LV myomectomy. Symptomatic improvement to NYHA functional class I or II was noted in 83% of patients surviving operation at a mean follow-up of 24 months, but longer follow-up will be necessary to see if improvement is sustained. Persistent functional class III symptoms after MVR are most likely secondary to decreased LV compliance, small vessel ischemia, or arrhythmias found in HCM. We believe that MVR is indicated in the operative treatment of HCM in select individuals, and that LV myomectomy is the operation of choice for those patients not fulfilling the criteria for MVR.

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DISCUSSION

DR D. CRAIG MILLER (Stanford, CA): Dr McIntosh, I'd like to start by complimenting you for your precautionary tone—which I don't think we'll hear from the lips of the next discussant, Dr Cooley—that MVR is solely a secondary procedure for the treatment of obstructive HCM. I also promise not to be as harsh as your ex-colleague, Ed Stinson, when he wrote not too long ago "Mitral valve replacement alone for [idiopathic hypertrophic subaortic stenosis (IHSS)] should be condemned on the basis of needless sacrifice of a normal mitral valve, exposure of the patient to the hazards of a prosthesis, with or without anticoagulation, and failure to address the primary anatomical abnormality."

On the other hand, when we as surgeons are asked to see patients with IHSS and high gradients, we should be circumspect. Only 25% of patients with HCM have the obstructive variety, and perhaps more importantly, this may basically be mostly a diastolic disease, not systolic. This LV diastolic dysfunction coupled with the additional important features of IHSS, such as microischemia, arrhythmias, heterogeneous atypical myocyte morphology, and easy ventricular tachycardia/ventricular fibrillation inducibility during electrophysiological induction studies, do limit the current role of operative treatment.

Eliminating the systolic gradient usually does not do much about the other problems; indeed, the biggest unanswered question with surgical treatment of IHSS is whether or not we can reduce the incidence of sudden death. It's going to be difficult to convince our cardiologists that we have a bigger role to play in the treatment of this disorder unless we can prove to them that the sudden death rate, which is usually quoted at 2 to 4 percent per patient-year (%/pt-yr) in medically-treated patients, can actually be reduced. This concern brings up the price that we pay if we are forced to resort to MVR.

The Stanford series, the overwhelming majority of whose patients were operated on by Ed Stinson, now numbers over 100 patients; transaortic LV myomectomy was the procedure of choice, and the late annualized incidence of cardiac death was 1.3

%/pt-yr. Late death could not be statistically predicted by any combination of variables that we assessed. Similar results have been demonstrated in previous reports from the NIH and recently in a large long-term study from the Mayo Clinic by Hartzell Schaff and his associates on patients after LV myomectomy. A rate of approximately 1.6 %/pt-yr, however, was also recently reported after MVR for IHSS by Dr Cooley's group. But, taking the liberty of extrapolating from the data provided in your manuscript, the annualized incidence of death in your particular patient population was approximately 5.5 %/pt-yr. Due to the limited extent of follow-up and the known high hazard phase of all morbid events early after a valve operation, this figure may well be an overestimate, which might therefore decline as more late follow-up accumulates. However, I don't think we're going to have an easy time convincing our cardiologists that MVR is the way to go if this is really the price our patients are going to have to pay.

You mentioned three reasons that mandated MVR instead of LV myomectomy. I might agree with you regarding the "atypical morphology" criterion. On the basis of the exquisite intraoperative, epicardial Doppler echocardiography resources you have in Bethesda, that may well be a real entity that maybe other groups just don't see. On the other hand, the majority of your cases were carried out due to the "thin septum" criterion. I feel compelled to ask why—especially with adjunctive intraoperative, epicardial color flow Doppler echocardiography—this should really be treated by MVR, which you agree is only a second choice surgical procedure? Are you perhaps just a little "gun-shy" after your paper published last year addressing the results of LV myomectomy in older patients (≥65 years) with coronary disease? In that report, the operative mortality rate was 27%, and all deaths were due to iatrogenic ventricular septal defects. You're certainly not talking about the same patients now; the patient group discussed today consisted of younger patients who did not have coronary disease.

Your third indication for MVR is when a previous LV myomectomy has been "inadequate," as judged by intraoperative Doppler echocardiography. Could you please elaborate for us how you define "inadequate" with regard to when you decide to do a second LV myomectomy versus MVR?

Looking at the late deaths, I'm a little concerned that you report that only 1 of the 6 was valve-related. We can't prove it one way or the other, but if you include the 1 sudden death and the 1 with a periprosthetic leak, we're actually talking about 4 or 5 of the 6 late deaths as possibly being valve-related; does this risk justify resorting to MVR? Furthermore, the linearized rate of all valve-related complications, again extrapolating from the data in your manuscript, is greater than 12 %/pt-yr.

Could you also please elaborate on how you are using the AICD in these patients? You mentioned in the manuscript that AICD patches were inserted in some individuals, but I could not determine how you selected these patients nor if AICD generators were later inserted. If so, on what basis was this decision made? Finally, what are the indications at the NIH currently for amiodarone treatment in patients with IHSS? Some in the audience may find this interesting, as amiodarone is apparently not used for its antiarrhythmic effects per se, despite the fact that it is very popular today for patients with HCM; it may actually be "proarrhythmic." Nevertheless, it's felt to be beneficial because it lowers heart rate, has negative inotropic properties, and may improve the severe diastolic LV relaxation abnormalities.

I compliment you again for your restraint, and agree that the primary surgical procedure of choice for patients with obstructive IHSS remains transaortic LV septal myomectomy.

DR DENTON A. COOLEY (Houston, TX): I was interested in Dr McIntosh's paper for several reasons and compliment him on his objectiveness while working in a setting where the method of surgical treatment had been firmly established and, more seemingly, beyond question or challenge.

When I reported our experience with MVR for this disease beginning in 1970, Dr Glenn Morrow, then chief of Surgery, influenced the chief of Pathology, Bill Roberts, to educate me and others as to why MVR was an unacceptable and poorly conceived treatment for IHSS. At times, their statements were highly critical and even emotionally charged. Thus, I can view these results from the Clinical Research Center with satisfaction and some amusement.

My colleagues, Drs Leachman and Krajcer, have reviewed our results with 269 patients treated surgically for IHSS, of which 80 patients (29%) underwent MVR. The remainder had septectomy as espoused by Morrow and his earlier disciples. Forty-two patients were female and 38 male; the mean age was 49 years.

Postoperative studies in the myomectomy group revealed resting outflow gradients of 69 mm Hg at rest before operation and 10 mm Hg after operation. Under provocation with Isuprel (Winthrop-Breon Laboratories, New York, NY), the average gradient was 135 mm Hg before operation and 35 mm Hg after operation.

In the patients undergoing MVR, the average preoperative resting gradient was 75 mm Hg; the postoperative gradient was 10 mm Hg. The important feature was that under provocation, the preoperative outflow gradient was 141 mm Hg, and after operation it was just 10 mm Hg. Therefore, it was not possible to evoke a pressure gradient in the patients who underwent MVR.

Survival in the two groups was roughly equal. There was an initial lower survival among the patients undergoing MVR, but that has not been our recent experience.

The conclusions that can be drawn from our study are that MVR does give substantial symptomatic improvement, dramatic improvement in LV outflow gradient at rest, and absent gradient even with provocation, as well as a reduced LV end diastolic pressure. There is a low operative and annual mortality. Improvement is obtained when septal myectomy has failed, and there is an acceptably low rate of complications. Myomectomy in addition to, or added to, an MVR did not seem to benefit the patient.

Finally, our experience confirms what we learned 20 years ago, that removing and replacing the mitral valve with a low-profile prosthesis eliminates the LV outflow pressure gradient.

Selection of patients for this more aggressive treatment, namely MVR, remains a matter of clinical judgment. In my opinion this procedure need not be used in every patient who is subjected to surgical treatment. Therefore, I'd like to ask Dr McIntosh, as this is a recent, consecutive series, what percentage of your patients underwent ventricular septectomy and what percentage had MVR? What is your procedure of choice at this time?

DR McINTOSH: I'd like to thank Dr Miller and Dr Cooley for their comments and their questions.

Dr Miller, first of all, inadequate LV myomectomy is assessed by intraoperative echocardiogram. It would mean that on the short-axis view we would demonstrate that the systolic anterior motion still contacts the septum in the area of the previously performed LV myomectomy. This situation would be amenable to performing another LV myomectomy. If, however, there is insufficient tissue left in the trough and there is still systolic anterior motion that strikes the back of the trough, I think there would be a high risk of a ventricular septal defect.

One of the things that I have noticed is that in some patients the mitral valve is redundant, perhaps secondary to myxomatous degeneration that causes excessive leaflet tissue in the LVOT, which may contact the trough. One of the things that I have done on patients in whom I think the LV myomectomy may be too shallow is to plicate the anterior leaflet of the mitral valve through the aortic annulus in the region of the scar, which is secondary to contact of the mitral valve on the septum.

The 1 patient that you mentioned who died of a periprosthetic leak did undergo repair at 8 months and died at 51 months after his MVR, of complications I think unrelated to his valve replacement.

Our procedure at this time for the implantation of the AICD is that the patient is brought back to our cardiology service 60 to 90 days after operation and undergoes an electrophysiological study at that time to determine whether significant ventricular arrhythmias are still present. If so, the AICD is implanted.

The major indication for amiodarone therapy in these patients is atrial fibrillation. We know that atrial fibrillation certainly will cause marked symptomatic deterioration in these patients with decreased ventricular compliance, and amiodarone has been found to be a very effective drug in maintaining sinus rhythm. So that is a major indication. We do use it as a negative inotrope to relieve the outflow tract obstruction as well.

Dr Cooley, I think of the last 225 patients that I have operated on, approximately 75% of the procedures have been LV myomectomies and 25% of them MVRs. My choice of operation at this time is always an LV myomectomy, if permitted.

I would like to thank The Society for the opportunity to present this information to them.

Notice From the American Board of Thoracic Surgery

The American Board of Thoracic Surgery began its recertification process in 1984. Diplomates interested in participating in this examination should maintain a documented list of the cardiothoracic operations they performed during the year prior to application for recertification. They should also keep a record of their attendance at thoracic surgical meetings, and other continuing medical education activities, for the 2 years prior to application. A minimum of 100 hours of approved CME activity is required.

In place of a cognitive examination, candidates for recertification will be required to complete both the general thoracic and cardiac portions of the SESATS III syllabus (Self-Education/Self-Assessment in Thoracic Surgery). It is not necessary for candidates to purchase SESATS III booklets prior to applying for recertification. SESATS III booklets will be forwarded to candidates after their applications have been accepted.

Diplomates whose 10-year certificates will expire in 1991 may begin the recertification process in 1989. This new certificate will be dated 10 years from the time of expiration of the original certificate. Recertification is also open to any diplomate with an unlimited certificate and will in no way affect the validity of the original certificate.

The deadline for submission of applications is July 1, 1989. A recertification brochure outlining the rules and requirements for recertification in thoracic surgery is available upon request from the American Board of Thoracic Surgery, One Rotary Center, Suite 803, Evanston, IL 60201.

Why Is the Lower Torso Protected in Traumatic Asphyxia?

A New Hypothesis

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Ray C.-J. Chiu, MD, PhD, FRCS(C)

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Traumatic asphyxia secondary to a crush injury of the chest is characterized by craniocervical cyanosis, subconjunctival hemorrhage, and severe vascular engorgement of the head and neck. These signs are believed to be due to high venous pressures causing stasis and capillary rupture. A "fear response" that produces a strong Valsalva maneuver is thought to be necessary for their development. The lower torso seems to be protected, and previously this was thought to be due to its superior system of valves. We present here ultrasonographic evidence that the inferior vena cava is compressed or obliterated during a Valsalva maneuver, and propose that this compression protects the lower torso during traumatic asphyxia.

(Ann Thorac Surg 1989;47:247–9)

The clinical syndrome of craniocervical cyanosis, subconjunctival hemorrhage, and severe vascular engorgement of the head and neck secondary to a crush injury of the chest has been called "traumatic asphyxia." It was described in 1837 by Ollivier [1], who noted these characteristic findings in patients trampled to death by crowds in Paris. He termed it the *masque ecchymotique*. The syndrome was further defined in 1900 by Perthes [2], who added mental dullness, hyperpyrexia, hemoptysis, tachypnea, and "contusion pneumonia" to the complex. Subsequently, more than 200 cases have been described and many other clinical signs have been added [3–8]. The vast majority of these signs occur in the upper torso. The lower torso seems to be protected.

The pathophysiology of traumatic asphyxia was studied experimentally in a canine model by Williams and colleagues [8] in 1967. They proposed that for the clinical syndrome to develop, the victim needed a warning so that he could close his glottis and brace his abdominal musculature—essentially a Valsalva maneuver. Without this "fear response," the elevated venous pressures and reflux of blood into the great veins of the head and neck could not be reproduced in spite of a severe crushing chest injury.

Like other investigators [2–7], Williams and associates [8] thought that the lower torso, unlike the upper half of the body, was protected from the elevated venous pressures by a series of valves. However, valves certainly are present in most of the great veins of the upper torso including the jugular, subclavian, and axillary veins [9], and their competence against physiological transvalvular pressure gradients has been demonstrated [10]. Why then is the lower torso protected in traumatic asphyxia? With this in mind, we sought an alternative explanation.

We propose that the elevated intraabdominal pressure that develops during the fear response (Valsalva maneuver) is directly transmitted to the inferior vena cava (IVC), thereby collapsing the IVC. We believe this will explain the protection of the lower extremities in traumatic asphyxia. To test the hypothesis that an increased intraabdominal pressure can obliterate or substantially reduce the lumen of the IVC, an ultrasonographic study was performed.

Material and Methods

Four normal male volunteers of average height and weight were examined sonographically with a real-time phased-array scanner (Toshiba SL-90). The IVC was visualized in both sagittal and transverse planes with the volunteers breathing normally and then during a Valsalva maneuver.

Results

In all 4 volunteers, the diameter of the IVC was found to vary with respiration. During expiration, it was the largest (Fig 1). During inspiration, it narrowed slightly. Finally, during a Valsalva maneuver, the IVC was observed to narrow and then collapse completely as the volunteer progressively increased the force of abdominal muscle contraction (Fig 2).

Comment

The signs of traumatic asphyxia are thought to be caused by the rupture of venules and capillaries by high venous pressures [8]. To develop these high pressures in the capacitance venous system, a substantial amount of blood

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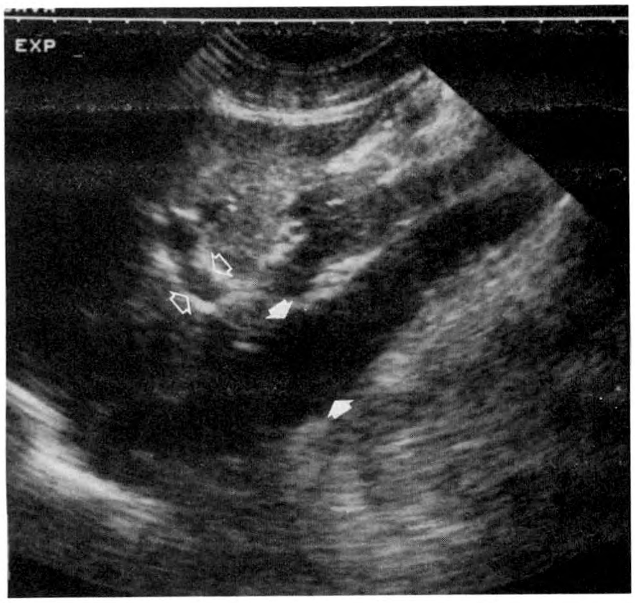

Fig 1. Sagittal view of inferior vena cava (solid arrows) *and portal vein* (open arrows) *during expiration.*

must be translocated. Therefore, there must be considerable retrograde blood flow to the upper torso. Why does this not occur in the lower extremities?

Flow through a collapsible tube that passes through a pressurized container is dependent on the inflow pressure, the outflow pressure, and the pressure in the container. As long as the outflow pressure is lower than the container pressure, flow will be proportional to the difference between the inflow pressure and the container pressure [11]. The IVC in the abdominal cavity represents just such a collapsible tube in a pressurized container.

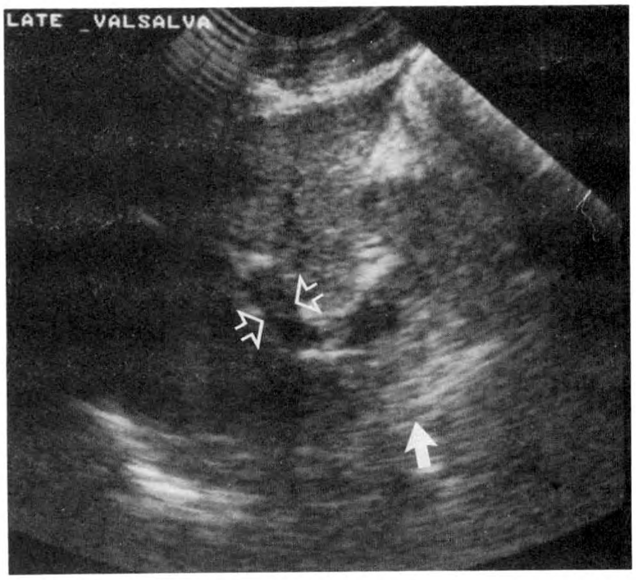

Fig 2. Sagittal view of inferior vena cava (solid arrow) *and portal vein* (open arrows) *during Valsalva maneuver. Note obliteration of the inferior vena cava.*

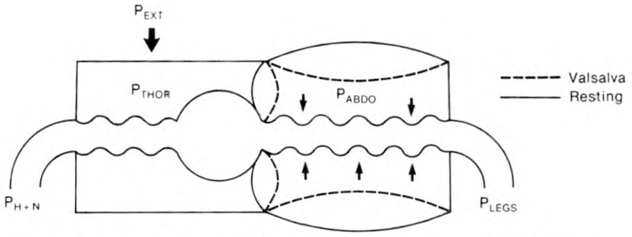

Fig 3. Hemodynamics in traumatic asphyxia. See text for details. (P_{ABDO} = *intraabdominal pressure;* P_{EXT} = *crushing pressure on chest;* P_{H+N} = *peripheral venous pressure in the head and neck;* P_{LEGS} = *peripheral venous pressure in the legs;* P_{THOR} = *intrathoracic pressure.)*

The peculiar hemodynamics of traumatic asphyxia are demonstrated in Figure 3. The crushing force (P_{EXT}) produces a raised intrathoracic pressure (P_{THOR}), which represents the driving pressure for retrograde venous blood flow out of the chest. The peripheral venous pressure (P_{PERI}), when a person is in the supine position, is equal in the upper and lower torsos. In the head and neck region, retrograde blood flow ($Flow_{H+N}$) is proportional to the difference between P_{THOR} and P_{PERI}:

$$Flow_{H+N} \ \alpha \ (P_{THOR} - P_{PERI}).$$

Because of the collapsible nature of the IVC, retrograde flow to the legs ($Flow_{LEGS}$) is proportional to the difference between P_{THOR} and the higher of the intraabdominal pressure (P_{ABDO}) and P_{PERI}. Clearly, if a victim does have a fear response, a tremendous increase in P_{ABDO} occurs, and this exceeds P_{PERI}. Therefore, $Flow_{LEGS}$ is proportional to (P_{THOR} − P_{ABDO}). As P_{ABDO} is greater than P_{PERI}, therefore, $Flow_{H+N}$ is greater than $Flow_{LEGS}$. Thus in the clinical syndrome of traumatic asphyxia, retrograde venous blood flow occurs preferentially in the upper torso. This leads to venous engorgement and capillary rupture in the craniocervical region, the *masque ecchymotique*.

Valves can play only a limited role in the protection of venous beds against very high pressure. Our study demonstrates that the elevated intraabdominal pressure developed during the fear response can collapse the IVC. We propose that this is the major pathophysiological mechanism for protecting the lower torso from the venous injury seen in traumatic asphyxia.

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Notice From the Southern Thoracic Surgical Association

The Thirty-sixth Annual Meeting of the Southern Thoracic Surgical Association will be held at the Phoenician Golf and Tennis Resort, Scottsdale, AZ, November 9–11, 1989. There will be a $155 registration fee for nonmember physicians except for guest speakers, authors and coauthors on the program, and residents. There will be a a $50 registration fee for attendees of the Postgraduate Course, which will be held the morning of Thursday, November 9, 1989. The Postgraduate Course will provide in-depth coverage of thoracic surgical topics selected primarily as a means to enhance and broaden the knowledge of practicing thoracic and cardiac surgeons.

Members wishing to participate in the Scientific Program should submit an original abstract and one copy by May 15, 1989, to Bradley M. Rodgers, MD, Program Chairman, Southern Thoracic Surgical Association, 111 East Wacker Drive, Chicago, IL 60601. Abstracts must be submitted on the Southern Thoracic Surgical Association abstract submission form. These forms may be obtained from the Association's office or in the March 1989 issue of *The Annals of Thoracic Surgery*. All slides used during the presentation must be 35 mm. Manuscripts of accepted papers must be submitted to *The Annals of Thoracic Surgery* prior to the 1989 meeting or to the Secretary-Treasurer at the opening of the Scientific Session.

Applications for membership should be completed by July 1, 1989, and forwarded to Hooshang Bolooki, MD, Membership Committee Chairman, Southern Thoracic Surgical Association, 111 East Wacker Drive, Chicago, IL 60601.

Gordon F. Murray, MD
Secretary-Treasurer
Southern Thoracic Surgical Association
111 East Wacker Drive
Chicago, IL 60601

Penetrating Wounds to the Heart: A Wartime Experience

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Division of Thoracic and Cardio-vascular Surgery, Hôtel-Dieu de France, Université Saint Joseph, Beirut, Lebanon

Forty-nine war casualties with penetrating cardiac wounds were treated at the Hôtel-Dieu de France University Hospital between April 1975 and December 1987. All the wounds were caused by high-velocity missiles. An aggressive approach was utilized. Emergency room thoracotomy was performed in 17 "lifeless" patients, 4 of whom survived. Twenty-seven of the 32 patients who were in stable enough condition to undergo initial repair in the operating room survived. Overall survival was 63% (31/49). No intracardiac injuries were diagnosed in survivors, and no cardiac reoperations were required. Careful analysis of the trajectory of the missile or missiles and a portable chest roentgenogram were the most important factors for diagnosing a penetrating wound to the heart and for predicting potential associated injuries.

(Ann Thorac Surg 1989;47:250–3)

One of the ultimate challenges for the surgeon is the management of a patient with a penetrating wound to the heart. Few injuries have as great potential to be life-threatening as damage to the heart. Precise recognition, aggressive resuscitation, early intervention, and meticulous and individualized operative techniques are essential to a high standard of success.

This review relates the experience of the Hôtel-Dieu de France University Hospital during the 12 years of war from 1975 to 1987.

Material and Methods

Between April 1975 and December 1987, there were 3,157 patients treated for penetrating thoracic injuries at the Hôtel-Dieu de France University Hospital, Beirut, Lebanon. Forty-nine (1.6%) of these patients were operated on for penetrating wounds of the heart. All were war casualties. There were 45 male and 4 female patients ranging in age from 16 to 48 years (average age, 25 years). All the wounds were caused by high-velocity missiles (greater than 500 m/s).

The war in Lebanon is an urban war; our hospital is 1 km from the battlefronts. Because of this particular location, most casualties reach the emergency area within 15 minutes of injury.

The management protocol remained unchanged over the period of the study. Every patient with a suspected cardiac injury arriving in the emergency room (ER) was resuscitated at once by a trained surgical team under the supervision of a senior resident and an attending general surgeon or a thoracic and cardiovascular surgeon with extensive experience with trauma patients. If the patient had no cardiac activity on admission or sustained arrest during resuscitation, an endotracheal tube was inserted and a left anterolateral thoracotomy was performed while the patient was on a stretcher; there was no skin preparation. Bleeding was controlled, and if the heart recovered, the operation was completed in the operating room (OR). If the diagnosis of cardiac wound was obvious, the patient was transferred to the OR. If the diagnosis was not clear, as in a patient with shock and multiple associated injuries, more investigations were carried out (chest roentgenogram, electrocardiogram [ECG], measurement of central venous pressure).

Rapid administration of lactated Ringer's solution was started on arrival in the ER until isogroup blood was available. Broad-spectrum antibiotics were routinely administered in the ER to all the war casualties.

The preferred method of opening the chest was a median sternotomy in the OR and a left anterior thoracotomy in the ER. The pericardium was opened longitudinally to avoid injury to the phrenic nerves. The cardiac wound was repaired with figure-of-8 sutures using silk 0. Teflon pledgets were used whenever the myocardium was friable. The pericardium was closed with an inferior window left to prevent tamponade. Pulmonary lacerations were treated as necessary, as were other associated injuries in the chest and abdomen. Pericardial and pleural drains were placed, and the sternum was closed with steel wires. Abdominal injuries were treated through a midline abdominal incision. During the early postoperative period, the patient was kept in the intensive care unit.

Results

Seventeen patients (35%) had no detectable cardiac activity on admission or sustained arrest soon after arrival and underwent thoracotomy in the ER (group 1). In the remaining 32 patients (65%), an expeditious history and physical examination were done before their transfer to the OR (group 2). Shock was a constant finding. Beck's triad of hypotension, venous distention, and muffled cardiac sounds was recorded in 16 patients (33%), and restlessness was present in 24 (49%). The most helpful method for raising suspicion of a cardiac wound was careful reconstruction of the trajectory of the projectile.

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Table 1. Associated Injuries

Associated Injury	No. of Patients
Lungs	
One	19
Both	11
Liver	9
Stomach	7
Spleen	6
Inferior vena cava	4
Colon	2
Small intestine	2
Other	2

A chest roentgenogram was obtained in all group 2 patients and was helpful in 25 (78%); it showed the exact location of the missile or missiles in 16 patients, an enlarged heart in 5, pneumopericardium in 2, and massive hemothorax in 7. Central venous pressure was recorded in the immediate preoperative period in 8 patients, and was elevated in 5. An ECG was made of 7 patients and was helpful in 2. Diagnostic pericardiocentesis and subxiphoid windows were not used.

Operative Findings

The most commonly injured cardiac chamber was the right ventricle (23 patients [47%]), followed by the left ventricle (15 patients [31%]), the right atrium (8 patients [16%]), and the left atrium (3 patients [6%]). There were no intracardiac injuries in the patients who survived. Injuries to the coronary arteries were noted in 3 patients: two to the distal left anterior descending coronary artery and one to the proximal circumflex coronary artery. Some degree of cardiac tamponade was found in 27 patients. In all group 1 patients there was a combination of tamponade and massive extravasation of blood in the thoracic cavity. Cardiopulmonary bypass was not used in this series.

Associated injuries were present in 28 patients, the most common being injury to the lungs. Table 1 lists the associated injuries.

Mortality and Morbidity

Of the 17 patients in group 1, 13 (77%) died. Among the 32 patients in group 2, 5 (16%) died. The causes of death are presented in Table 2.

The most common postoperative complication was lung atelectasis. Two patients who had ligation of the distal left anterior descending coronary artery sustained a myocardial infarction. No serious wound sepsis was recorded.

The average hospitalization was 21 days.

Follow-up

All patients are seen regularly and are examined clinically and with echocardiography. Follow-up averages 52 months (range, 11 to 113 months). No cardiothoracic problems have been noted, and no reoperations on the heart or thorax have been required.

Comment

Several factors are involved in the selection of patients who survive a cardiac injury and reach medical attention [1–13]. Among these factors are the time taken to reach the hospital, the weapon used, the size of the myocardial injury, the injured cardiac chamber, the presence of coronary artery damage, the presence of tamponade, and associated injuries. In the small group who reach the hospital, the most important factors for survival are active resuscitation, fast diagnosis, and immediate intervention as well as diagnosis and treatment of the associated injuries [1–6, 11, 13].

Wartime injuries deserve special consideration, for high-velocity missiles often inflict substantial tissue damage to the heart and to the adjacent great vessels, lungs, and upper abdominal organs, thus making it very difficult for the victims to stay alive [14, 15]. This is reflected by the fact that among 3,157 patients treated for thoracic injuries in our hospital, only 1.6% sustained cardiac wounds. The classic 20% to 50% incidence of survivors who reach medical care reported in civilian practice [1–6, 9] tends to be much lower in wartime, mainly because of the massive tissue loss and the serious associated injuries. Also, gunshot wounds seen in civilian patients are usually caused by handguns and hunting rifles, which are much less powerful than the modern weapons used during wartime; thus the injuries are less serious.

In this series, shock was a constant clinical finding (100% of patients). However, 3 of the patients who were wounded inside the hospital and were seen a few minutes after the injury were completely asymptomatic. Blood pressure was normal on admission, and shock appeared later.

Beck's triad, which is considered pathognomonic for tamponade [1, 12], was found in 33% of the patients and in 60% of the patients with proven tamponade.

A raised central venous pressure was recorded in 5 of the 8 patients in whom it was measured. However, this variable does have limitations as a result of several conditions such as restlessness, profound shock, hemopneumothorax, and malposition of the tip of the catheter.

Pulsus paradoxus was noted in 4 of the 13 patients in whom it was sought.

Careful reconstruction and analysis of the trajectory of the missile using the entrance wound, the exit wound, and the chest roentgenogram proved to be the most useful for detecting cardiac injury.

Table 2. Causes of Death[a]

Cause	No. of Patients
Died in emergency room[b]	8
Multiple-organ failure	8
Intraabdominal complications	3
Coma and neurological complications	2
Died in operating room[c]	2

[a] Multiple causes were present in most patients. [b] Irreversible cardiac arrest. [c] Uncontrollable bleeding or serious irreversible damage.

A portable chest roentgenogram was of great value when studying a patient with a suspected cardiac injury and in whom the missile did not leave the body or who was injured by several missiles. However, this roentgenogram should be made under strict surveillance and while active resuscitation is underway. It is only under these conditions that a chest roentgenogram can be safely obtained in a seriously injured individual and in a matter of minutes, for no valuable time should be wasted. The chest roentgenogram is also helpful in predicting associated injuries such as thoracoabdominal wounds, which, when overlooked, will increase patient mortality and morbidity even if the cardiac repair was successful.

The ECG might be of some value and should be reserved for patients in fairly stable condition [1, 9, 12]. Although it is of great value for some situations [3, 7], no place was found for pericardiocentesis, either as a diagnostic or therapeutic procedure [6, 8].

Subxiphoid windows have been advocated as a diagnostic procedure for tamponade [3, 16–21]. We have never used this procedure, for we believe it is time-consuming, potentially dangerous, and of no real benefit in the case of war injuries to the heart.

Cardiorrhaphy is now considered the only procedure for the treatment of a cardiac injury. Ludwig Rehn performed a successful cardiorrhaphy on September 9, 1896 [21]. Bigger in 1939 and Blalock in 1943, both greatly influenced by the high mortality associated with the surgical management of cardiac injuries, advocated conservative management of heart wounds [21]. Controversy concerning operative versus nonoperative treatment of cardiac wounds increased during the 1950s and 1960s. However, with the emergence of cardiac surgery and the dramatic decline in operative mortality, cardiorrhaphy was universally embraced in the literature as the procedure of choice for cardiac wounds [2, 3, 5, 7, 8, 10].

Median sternotomy was the preferred incision in this series, although some authors prefer a left anterolateral thoracotomy [8, 18, 19]. The advantages of the former include a bloodless field, good exposure of the heart and the two thoracic cavities, less postoperative pain, and fewer pulmonary complications. Also, a median sternotomy is easily extended to a midline laparotomy when necessary. A left anterior thoracotomy, on the other hand, can be performed more rapidly, and was reserved for patients in group 1.

The management of a severed coronary vessel remains controversial [12]. Some authors [3, 16, 19] advocate ligation; others recommend repair either while the heart is still beating [9–11], or after induction of cardiac arrest by lifting the heart or immediately initiating cardiopulmonary bypass [1, 5, 7]. We ligated all three severed coronary arteries we encountered. The 2 patients in whom the distal left anterior descending coronary artery was ligated showed signs of a limited myocardial infarction on the postoperative ECGs. In the third patient, the proximal circumflex coronary artery had been severed. It was ligated, but the patient died in the OR because of the cardiac injury and serious associated injuries.

No intracardiac injuries were noted in survivors, all of whom underwent electrocardiographic and echocardiographic studies. When dealing with cardiac wounds caused by high-velocity missiles, intracardiac injuries are rare in clinical series and more frequent in autopsy series, as the combined insult of such an injury and the heart wound itself is invariably fatal. None of the survivors has required reintervention for a cardiac cause.

Thirteen of the 17 patients undergoing thoracotomy in the ER (group 1) died. This 77% mortality seems very high compared with other reported series [5, 9, 13]. However, it can be explained by the fact that ER thoracotomy in our series was reserved for "lifeless" patients with no cardiac activity, whereas other authors [22–24] advocate this procedure when systolic pressure remains lower than 60 mm Hg for five to ten minutes despite treatment. This makes the interpretation of survival figures difficult.

In group 2, 5 patients (16%) died between three and 45 days postoperatively. These 5 patients were in profound shock on arrival, and although the heart recovered, they had sustained multiple-organ failure and could not survive.

In conclusion, patients with cardiac wounds who arrive at the hospital are rare during wartime. We have operated on 49 war casualties who sustained cardiac injuries from high-velocity missiles. Seventeen patients with no cardiac activity on admission had ER thoracotomy, 4 of whom survived. Thirty-two patients were operated on in the OR, and 27 survived.

This study has led us to the following four conclusions. (1) The most important steps in diagnosing a cardiac injury are careful analysis of the trajectory of the missile and examination of the preoperative chest roentgenogram. (2) Potential penetrating cardiac wounds caused by high-velocity missiles should be managed aggressively. (3) Emergency room thoracotomy is advocated only for lifeless patients or those whose condition is deteriorating. It should be the exception rather than the rule. (4) Associated injuries play an important role in the prognosis for these patients.

We thank Hala Zoghbi, BA, who prepared the manuscript, and John Relland, MD, who reviewed it.

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Correction of Aortico–Left Ventricular Tunnel During the First Day of Life

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Two critically ill newborns with aortico–left ventricular tunnel and severe heart failure were operated on at six and 14 hours after birth. The diagnosis was established clinically by the auscultatory finding of systolic and diastolic murmurs and by two-dimensional and Doppler echocardiography. In the first newborn, the left aortic sinus was connected with the left ventricle below the aortic valve by an aneurysmatically dilated tunnel. In the second patient, the tunnel connected the right aortic sinus and the left ventricle. The repair was performed under deep hypothermia, total hemodilution, and cardiopulmonary bypass. The tunnel was closed with two patches of Gore-Tex on the aortic and ventricular orifices. Both children are free from symptoms and are developing normally 10 and 8 months after repair.

(Ann Thorac Surg 1989;47:254–6)

A tunnel between the aorta and the left ventricle is a very rare congenital heart defect. It can cause severe aortic insufficiency in newborns. There are about 50 published reports of newborns having operation for this rare condition. In half, the condition was recognized clinically within the first days of life. Most of those newborns in whom the signs of severe heart failure appeared on the first day of life died without operation [1–4]. Only a few authors [5–7] have described successful operations on newborns. We present the cases of 2 newborns with aortico–left ventricular tunnel who underwent repair at six and 14 hours after birth.

Material and Methods

Patient 1

The first newborn (birth weight, 4,000 g) was admitted to our unit four hours after birth in critical condition. He was cyanotic with tachycardia (170 beats per minute), systolic and diastolic murmurs at the apex, an enlarged liver, and cardiomegaly on the chest roentgenogram.

The electrocardiogram (ECG) showed left ventricular hypertrophy with strain and ischemia. Two-dimensional echocardiography demonstrated dilatation of the left ventricle with an almost akinetic hypertrophied free wall. The aorta was markedly dilated. A tunnel passed from the left aortic sinus to the left ventricle below the aortic valve (Fig 1A). A small defect in the muscular trabecular part of the ventricular septum was also seen. Massive aortic regurgitation through the tunnel into the left ventricle was shown by Doppler study (Fig 1B), and a wide opened ductus arteriosus with a right-to-left shunt was also demonstrated.

Because of severe congestive heart failure, the neonate underwent closure of the tunnel six hours after birth. Cardiopulmonary bypass with reduced blood flow under deep hypothermia (18°C) was used. Total hemodilution was achieved with the Capiox II 08 capillary membrane oxygenator (Terumo Corp, Tokyo, Japan). The large patent ductus arteriosus was ligated before the initiation of cardiopulmonary bypass.

The lesion was localized in the aortic root posterior to the main pulmonary artery and in front of the left atrial appendage. It was a thin-walled, aneurysmal canal with a lumen of 10 mm (Fig 2A). After the cross-clamping of the aorta and the infusion of cold crystalloid St. Thomas's cardioplegic solution, the aorta was opened transversely. The aortic valve leaflets were fine and competent. The left aortic sinus was dilated and filled with myxomatous, membranous structures similar to valve tissue. At the bottom of this aortic sinus was a wide communication (15 × 15 mm) with the left ventricle. The left coronary artery originated from the inner side of the aneurysmal tunnel near its aortic orifice.

The aortic orifice of the tunnel was closed with a 7 × 7-mm Gore-Tex patch using a continuous suture of 6-0 Prolene. The tunnel was then opened, and the ventricular orifice was closed with another Gore-Tex patch (10 × 15 mm). The lumen of the tunnel was obliterated by stitches. The hemodynamically insignificant ventricular septal defect was not closed.

Patient 2

The second newborn (birth weight, 2,900 g) was cyanotic and hypotonic from birth. The roentgenogram showed cardiomegaly. The patient was referred to our unit seven hours after birth with suspected transposition of the great arteries.

On admission, a rough systolic murmur and a soft diastolic murmur were heard over the precordium. On the roentgenogram, the heart shadow filled nearly the whole chest. The ECG showed left ventricular hypertrophy. Echocardiography demonstrated substantial dilata-

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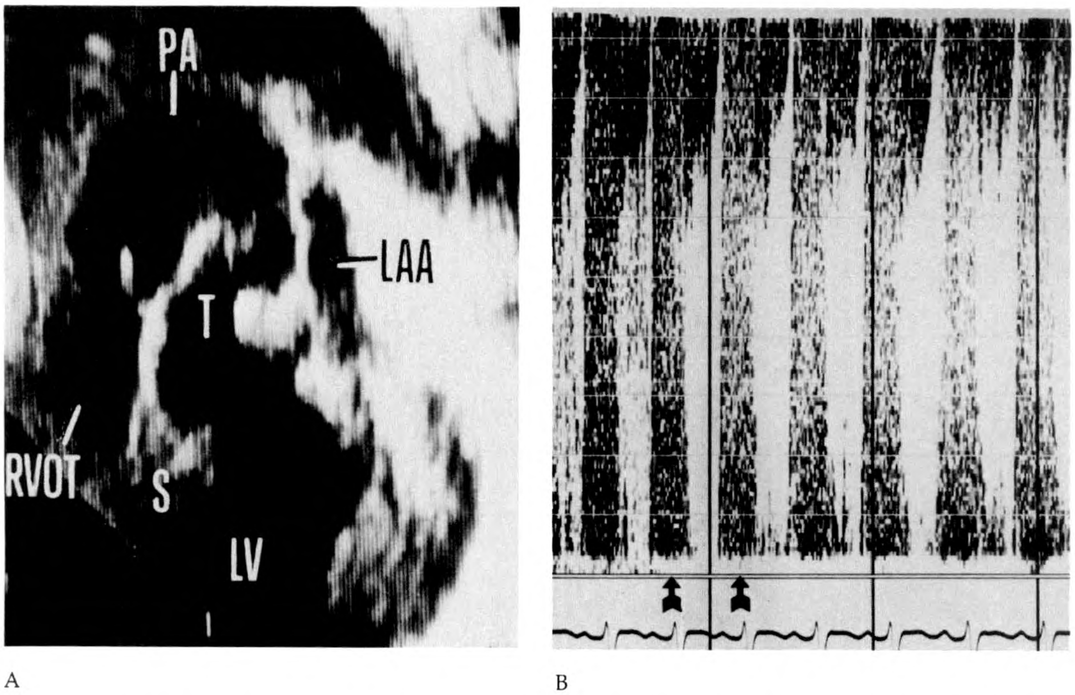

Fig 1. (A) Precordial sagittal cross section of echocardiographic investigation in patient 1. The tunnel (T) *arises from the left aortic sinus and passes between the pulmonary artery* (PA) *and the left atrial appendage* (LAA). *It enters the left ventricle* (LV). (RVOT = *right ventricular outflow tract;* S = *interventricular septum.) (B) Pulsed Doppler tracings showing diastolic regurgitant flow* (black arrows) *detected in the tunnel from the subcostal approach in patient 1. In systole, there is a lower velocity flow in the opposite direction toward the aorta.*

tion of the left ventricle and the aorta. The posterior wall of the left ventricle was contracting poorly. A tunnel from the right aortic sinus into the left ventricle with massive regurgitation was visualized (Fig 3). The ductus arteriosus was widely patent.

The patient underwent operation 14 hours after birth because of severe heart failure. The operation was performed during cardiopulmonary bypass using deep hypothermia (17°C), cold cardioplegic cardiac arrest, and total circulatory arrest. The ductus arteriosus was ligated at the beginning of perfusion. The lesion was seen on the anterior wall of the dilated aortic root; it protruded above the right aortic sinus (see Fig 2B). Through a transverse aortotomy, the tunnel orifice, 8 mm in diameter, was seen above the right aortic sinus. The tunnel led between the aorta and the main pulmonary artery to the left ventricle below the aortic valve. A Gore-Tex patch was placed from the aorta into the aortic origin of the tunnel. Through the opened canal of the tunnel, a second patch was sutured into the ventricular orifice of the tunnel (Fig 4).

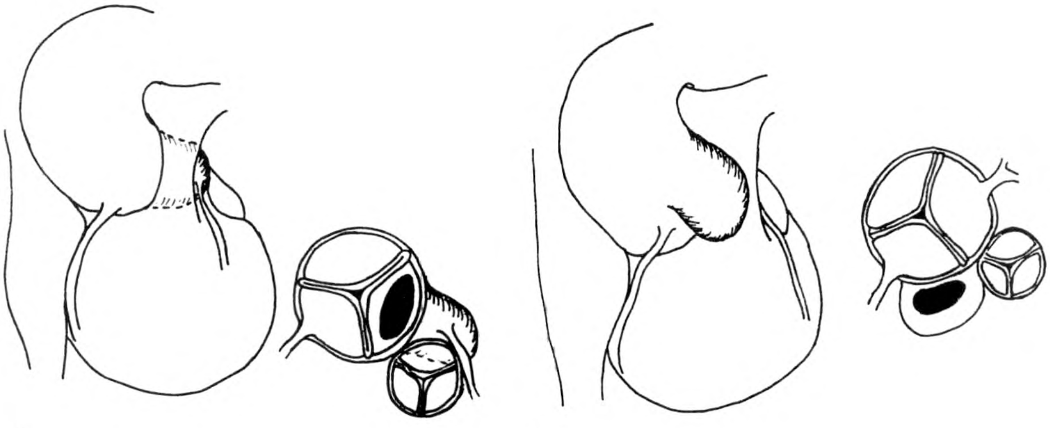

Fig 2. (A) Aortico–left ventricular tunnel in patient 1. The tunnel passes from the left aortic sinus, behind the main pulmonary artery, and in front of the left atrium. (B) Lesion in patient 2. The tunnel originates above the right coronary artery ostium and runs from the right aortic sinus in front of the main pulmonary artery.

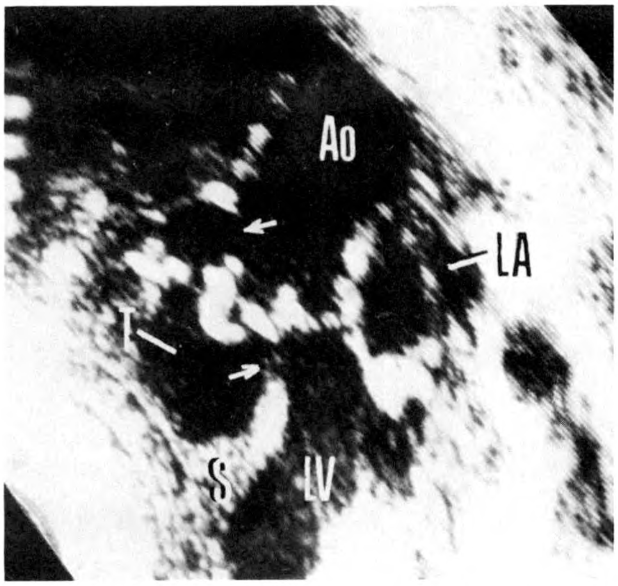

Fig 3. Precordial long-axis echocardiographic view of patient 2. The tunnel (T) *passes from the right aortic sinus* (upper arrow) *to the left ventricle* (LV) *below the aortic valve* (lower arrow). *(Ao = aorta;* LA *= left atrium;* S *= interventricular septum.)*

Results

The postoperative course of both newborns was uncomplicated. They were discharged home on the 15th and 20th postoperative days. Left ventricular dimension and function were normal on echocardiographic follow-up 3 months after operation in the first patient. Radionuclide angiocardiography showed good function of the left ventricle with a normal ejection fraction (ejection fraction = 0.76). The baby is well 10 months after operation.

The dimension and function of the left ventricle (studied echocardiographically) improved within 2 weeks after operation in the second patient. The baby is doing well at the age of 8 months.

Comment

Repair of aortico–left ventricular tunnel in infants has been described by several authors [4, 5, 8–10]. Correction has been performed in newborns by Björk [5], Fripp [6], Turley [7], and their associates.

The diagnosis can be established clinically, but cardiac catheterization and angiocardiography are generally considered necessary to confirm the diagnosis [5–7, 9, 11, 12]. We were able to confirm the clinical diagnosis by two-dimensional echocardiography and Doppler examination. We believe that invasive investigation is not necessary to establish the diagnosis in the critically ill newborn. We were confident that we could proceed with the operation on the basis of noninvasive studies.

Early operation is mandatory; without operation, many patients die during the first few days of life [1, 3, 4, 10].

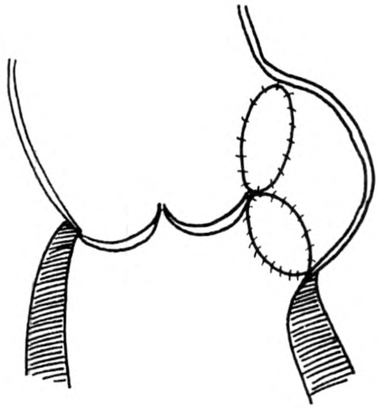

Fig 4. Operative approach with the two Gore-Tex patches. One patch closes the aortic orifice of the tunnel and the other, the ventricular orifice.

We used two patches to close both the aortic and ventricular ends of the tunnel. This technique should prevent further dilatation of the tunnel, which may be aneurysmal at birth.

We thank Dr Jaroslav Stark for his assistance in the preparation of this manuscript.

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Cryosurgical Ablation of Accessory Atrioventricular Pathways Without Cardiopulmonary Bypass: An Epicardial Approach for Wolff-Parkinson-White Syndrome

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An epicardial approach has been developed and applied to 31 Kent bundles (23 parietal, 1 right anteroseptal, and 7 posteroseptal bundles) in 28 patients with Wolff-Parkinson-White syndrome. Our technique consists of dissection of the atrioventricular fat pad of the Kent bundle site using an ultrasonic aspirator and subsequent cryosurgical ablation. For the left parietal and posteroseptal pathways, the apex of the heart has to be retracted upward, but this maneuver was well tolerated in all patients. Moreover, even through a narrow operative field, the ultrasonic aspirator permitted deliberate dissection on the beating heart without injury to major coronary vessels or the atrial wall. In 89% of the patients, operation was performed without the use of heart-lung bypass. All patients were free from preexcitation. With this technique, all Kent bundles except that adjacent to the atrioventricular node can be ablated on the beating heart, usually without heart-lung bypass.

(Ann Thorac Surg 1989;47:257–64)

The surgical technique for ablation of accessory atrioventricular (AV) pathways of the Kent bundle in Wolff-Parkinson-White (WPW) syndrome was developed by the pioneering work of Sealy [1], Iwa [2], and their associates. This standard procedure can be called the "endocardial approach," a technique in which the Kent bundles are divided from the endocardial side using cardiopulmonary bypass. This open heart approach has been performed routinely with low mortality and morbidity and a high success rate [3, 4].

In 1984, Guiraudon and colleagues [5] reported a new "closed heart" technique, which consisted of mobilization of the AV fat pad and subsequent cryoablation from the epicardial side. Their technique has the obvious advantage that the Kent bundles can be ablated without an atriotomy. The technique also obviates the inherent risk and morbidity related to aortic cross-clamping and cold cardioplegic cardiac arrest. More importantly, continuous monitoring of conduction over the AV and accessory pathways during dissection and cryosurgery is possible. This helps protect normal AV conduction and enables the surgeon to see preexcitation disappear during the course of the procedure. However, the operations by Guiraudon and co-workers [6] were performed during normothermic cardiopulmonary bypass in more than 90% of the patients, and morbidity due to a long period (sometimes more than 150 minutes) of normothermic extracorporeal circulation could not be avoided.

An epicardial approach has been developed at our institution independently of Guiraudon and co-workers, and has been applied to clinical cases since 1983 with a good success rate [7, 8]. Basically our technique is in line with that of Guiraudon and colleagues. However, by using an ultrasonic aspirator, which makes safe and easy AV fat pad dissection possible, most of our patients, including those with the left free wall and paraseptal types of pathway, could be operated on without extracorporeal circulation.

The purpose of this report is to describe our experience with 28 consecutive patients who underwent successful Kent bundle ablation using this epicardial approach.

Material and Methods

Patients

Of the 43 patients with WPW syndrome who have been operated on at our institution, the 28 consecutive patients who underwent operation with the epicardial approach between November 1984 and April 1988 constitute the basis of this report. Twelve of the remaining 15 patients were operated on with the classic endocardial approach before 1984. Since 1984, we have adopted the epicardial approach for almost all patients having operation for WPW syndrome. Three patients have been excluded from this strategy. One of them had Ebstein's anomaly, and in the other 2, the Kent bundles were determined by preoperative endocardial mapping to be located just adjacent to the AV node. The endocardial approach was selected for these 3 patients.

The clinical and electrophysiological profiles of the 28 patients operated on with the epicardial approach are

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Table 1. Clinical and Electrophysiological Characteristics of 28 Patients with WPW Syndrome Undergoing Operation by Epicardial Approach[a]

Variable	No.
Female : Male	14 : 14
Age (yr)	13–67 (37.3 ± 15.5)[b]
Type of clinical arrhythmia	
PSVT	9
PSVT + pseudoVT	19
Clinical symptoms	
Palpitations	7
Palpitations + dizziness or syncope	18
Palpitation + dyspnea	3
ERP of Kent bundle (ms)	240–360 (280 ± 34.0)[b]
Shortest R-R interval in spontaneous and/or induced AF (N = 23) (ms)	160–300 (233 ± 47.4)[b]
R-R interval < 240 ms	21 (75.0)
Medical refractoriness or intolerance	24 (85.7)
Concurrence with organic heart disease	3 (10.7)
ASD	1
VSD	1
DCM	1

[a] Numbers in parentheses are either the mean ± the standard deviation or percentages. [b] Mean ± standard deviation.

AF = atrial fibrillation; ASD = atrial septal defect; DCM = dilated cardiomyopathy; ERP = effective refractory period; pseudoVT = pseudoventricular tachycardia; PSVT = paroxysmal supraventricular tachycardia; VSD = ventricular septal defect.

summarized in Table 1. There were 14 female and 14 male patients, aged 13 to 67 years (mean age, 37.3 years).

Twenty-one patients (75.0%) were classified as "high-risk," which by our definition means that the atrium is vulnerable to atrial fibrillation and/or flutter and that the shortest R-R interval during spontaneous or induced atrial fibrillation and/or flutter is less than 240 ms. Five patients who were not in the high-risk category either had medically refractory tachyarrhythmias or could not adhere to any drug regimen because of intolerable side effects. Two patients were selected for operation because of associated cardiac anomalies (atrial septal defect and ventricular septal defect) that needed surgical correction. One high-risk patient had complications with dilatated cardiomyopathy and experienced congestive heart failure during the episodes of tachycardia. All 28 patients underwent extensive preoperative electrophysiological study to (1) confirm the presence and the electrical characteristics of the accessory pathway or pathways that participated in the genesis of clinical tachyarrhythmias, (2) localize the site of the accessory pathway or pathways, (3) check the atrial vulnerability to atrial fibrillation and/or flutter when necessary, and (4) assess the efficacy of drugs (see Table 1).

Figure 1 illustrates the sites of the accessory pathways in the 28 patients. There were 31 Kent bundles: 9 right free wall accessory pathways, 14 left free wall pathways, 1 right anteroseptal pathway, and 7 posteroseptal pathways. Three patients (10.7%) each had 2 accessory pathways. All sites of the pathways were precisely determined by preoperative endocardial mapping in the electrophysiological study and were confirmed by intraoperative epicardial mapping. No extra Kent bundles were found intraoperatively or postoperatively.

Surgical Technique

The heart was exposed through a median sternotomy except in 3 young women with a left parietal pathway. In these patients, the heart was entered through a left thoracotomy for cosmetic reasons. A median sternotomy was the main incision used because of the possible existence of an accessory pathway on the contralateral side that had not been detected in the preoperative electrophysiological study and would be inaccessible if the heart were entered through a thoracotomy.

After pericardiotomy, intraoperative epicardial mapping was performed to identify the area harboring the accessory pathway. We developed and used an on-line minicomputer system (modified HPM-6500; Fukuda Den-

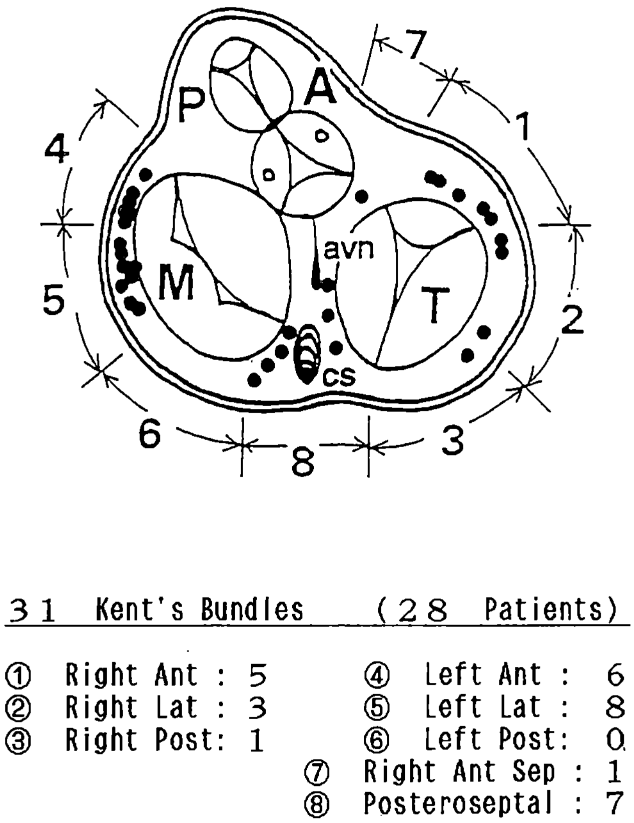

Fig 1. Localization of accessory atrioventricular pathways shown in a superior view of the heart with the atria cut away. Closed circles indicate sites of accessory pathways in 28 patients. Accessory pathway sites were classified into eight sections. There were 31 pathways: 9 right free wall, 14 left free wall, 1 right anteroseptal, and 7 posteroseptal pathways. (A = aortic root; avn = atrioventricular node; cs = ostium of coronary sinus; M = mitral valve; P = pulmonary trunk; T = tricuspid valve.)

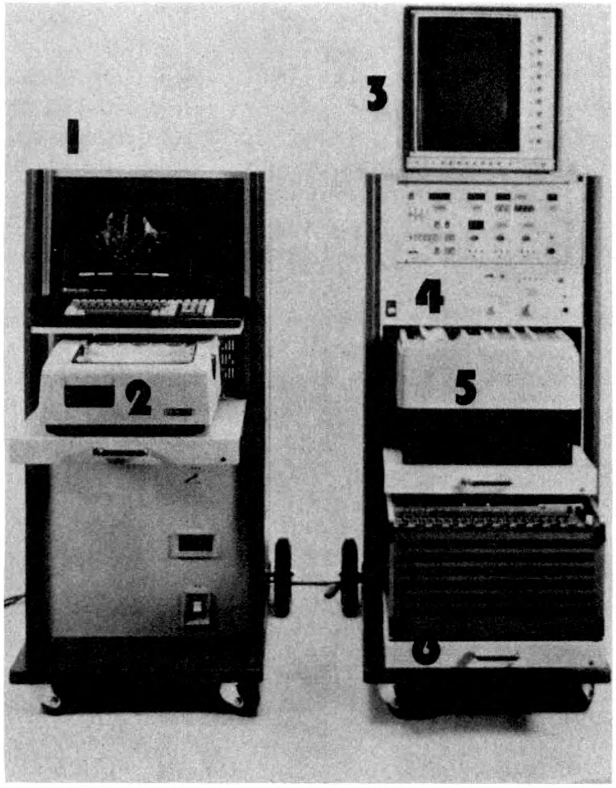

Fig 2. The on-line computerized intraoperative mapping system used at our institution (modified HPM-6500; Fukuda Denshi Co, Ltd, Tokyo, Japan). With this portable on-line computer system, both single-point mapping and multiple-point (up to 20 points) simultaneous mapping are possible. (1 = cathode-ray tube and minicomputer unit; 2 = hard-copy printer; 3 = polygraph for analog data display; 4 = stimulator for programmed electrical stimulation; 5 = thermal printer for analog data recording; 6 = 20-channel data tape recorder.)

shi Co, Ltd, Tokyo, Japan) for intraoperative mapping studies (Fig 2).

A ventricular epicardial excitation sequence map was acquired by measuring the conduction time difference for 51 predetermined points on the whole ventricular surface using a handheld roving bipolar electrode (distance between the bipolar pair = 1 mm). The measured data were instantaneously digitized and computed in the central processing unit of the HPM-6500 to be displayed as an isochronous map in real time so that the excitation sequence could be displayed on the cathode-ray tube almost as soon as the measurement was completed. With this system it took only approximately ten minutes on average to get a ventricular excitation map.

The area of ventricular insertion of the accessory pathway could be determined by this ventricular mapping during sinus rhythm or on atrial pacing (Fig 3); the atrial insertion site can be localized by atrial paraannular mapping performed during induced supraventricular tachycardia or on ventricular pacing. Recently a multichannel signal-processing unit was incorporated in the HPM-6500; consequently, with the use of a sock electrode loaded with 20 scattered bipolar pairs and a catheter electrode with six bipolar pairs, both a ventricular map and a paraannular map can be obtained on a few cardiac contractions (theoretically on one beat).

After the approximate site of the accessory pathway was determined by the global surface mapping procedure, the AV groove fat pad of the Kent bundle site was mobilized and dissected. We used an ultrasonic surgical aspirator (Sonotec; Sumitomo Bakelite Co, Ltd, Tokyo, Japan) for this purpose. Ultrasonic energy delivered from the tip of the bar microvibrating with a frequency of approximately 25 kHz dissipated and emulsified the fat tissue (which was aspirated through the lumen of the bar) while sparing resonating elastic blood vessels as long as the amplitude of vibration was within an appropriate range. This instrument enabled us to meticulously dissect the AV groove fat pad by simply stroking the fat pad surface gently until the valve annulus was exposed from the outside. This involved no risk of injuring major coronary vessels. Dissection usually took no longer than 20 minutes.

Thereafter, precise annular mapping was performed in the dissected AV groove using a catheter electrode with multiple bipolar pairs or a bipolar roving electrode. With this technique, almost pinpoint determination of the site of the accessory pathway was possible.

The area exactly determined to harbor the accessory pathway by annular mapping was subsequently cryosurgically ablated at a temperature of either −60°C or −150°C with an instrument utilizing liquid nitrogen as a coolant (Cryobar; Torisha Co, Ltd, Tokyo, Japan) (see Comment section for cryoablation temperature). As long as the "correct" area was dissected and cryoablated, disappearance of preexcitation would be seen by continuously monitoring the electrocardiogram within a minute of cryosurgery or even with dissection only. However, as mere disappearance of the delta wave does not always mean permanent destruction of the pathway, we have made it a rule to continue applying the cryoprobe for at least two minutes after the disappearance of preexcitation.

As a reinforcement, because of the possible existence of pathway or pathways nearby or an arborizing termination of the pathway [9], we usually extended the cryolesion 2 cm on each side of the point of the earliest excitation. During cryosurgery, the coronary arteries were deliberately shifted away to avoid involvement in the cryolesion (see Comment section). Figure 4 shows the cryoablation of the right anterior accessory pathway with our epicardial approach.

After the cryoablative procedure, the epicardium of the dissected site was usually loosely closed. However, the patients in whom the exposed annulus was left unclosed had no bleeding problem postoperatively.

Approaching the heart through a median sternotomy made dissection and cryoablation rather difficult for left free wall and posteroseptal accessory pathways, so the apex of the heart had to be lifted to get better exposure. Because most patients had normal cardiac function with good functional reserve, upward retraction of the apex did not cause major hemodynamic instability in general. Sometimes blood pressure was initially lowered, but it

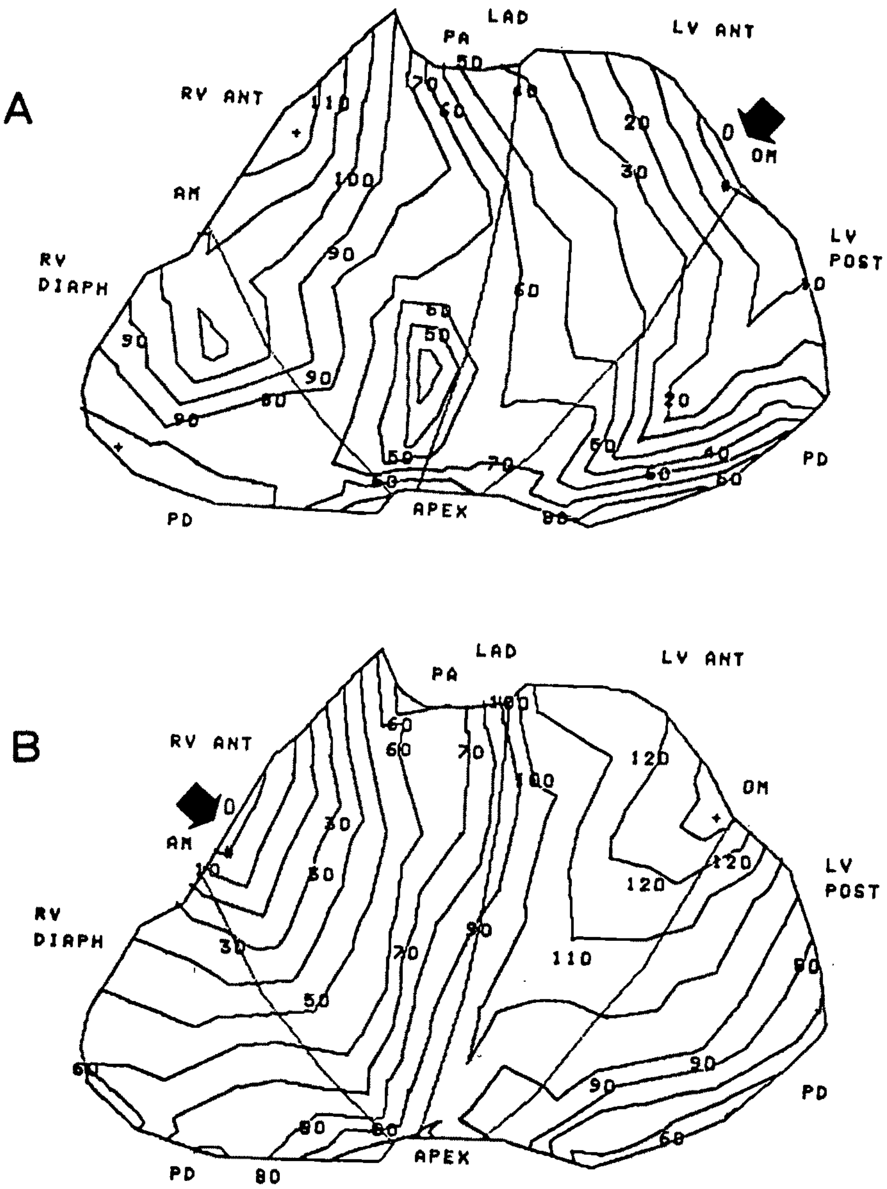

Fig 3. Hard copy of color graphics terminal display showing an isochronous contour map of the ventricular surface recorded intraoperatively using HPM-6500 (Fig 2). Local activation of 51 predetermined points on the whole ventricular surface was determined on a point-by-point basis with the handheld roving electrode. (A) Isochronous map of a patient with a left lateral accessory pathway. (B) Map of a patient with a right lateral accessory pathway. Time zero is the earliest point, and the isochronous interval is 10 ms. (AM = *acute margin;* ANT = *anterior;* DIAPH = *diaphragmatic surface of ventricle;* LAD = *left anterior descending coronary artery;* LV = *left ventricle;* PA = *pulmonary artery;* PD = *posterior descending branch of coronary artery;* POST = *posterior;* OM = *obtuse marginal branch;* RV = *right ventricle.)*

returned to normal within minutes because of reflex vasoconstriction. Also, the ultrasonic surgical aspirator allowed simple and easy dissection of the AV groove fat pad on the vigorously beating heart without the risk of injury to major coronary vessels or the fragile atrial wall, even when the exposure of the AV groove was limited (left free wall or posteroseptal accessory pathways) (Fig 5).

All patients tolerated the mapping, dissection, and cryoablation procedures quite well. Except for the procedures in 3 patients who required the endocardial approach, all operations were performed without the use of cardiopulmonary bypass.

Results

There were no operative deaths. Twenty-eight of the 31 accessory pathways were successfully divided at the initial operation. In 3 patients (10.7%), early recurrences necessitated reoperation. In these 3 patients (2 with a left lateral pathway and 1 with a right anterior pathway), the delta wave reappeared within 12 hours postoperatively. Epicardial mapping during the reoperation localized the accessory pathway at the same site as in the first operation, and all three pathways were successfully eliminated.

Kent bundles could be divided by the epicardial approach alone in 25 (89.3%) of 28 patients, but in 3 patients, as already mentioned, the endocardial approach was also required for successful division. In 1 patient with a left lateral wall pathway, the bar of the ultrasonic aspirator was inadvertently struck against the left atrial wall, thus tearing the wall. The wound was repaired with a suture with pledgets. These pledgets hindered application of the cryoprobe from the outside. Consequently, a classic endocardial ablation of the pathway was performed with cardiopulmonary bypass during aortic cross-clamping with cold cardioplegic cardiac arrest.

In 1 patient with bilateral free wall accessory pathways, the right pathway was easily divided by the epicardial approach. The left one, however, quickly revived after several applications of the cryoprobe (−60°C), so we changed to the endocardial approach with success.

In 1 patient, epicardial mapping showed that the pathway was on the right side of the crux. Thorough dissection of the pyramidal fat pad tissue around the crux followed by application of the cryoprobe (−150°C) failed to ablate the accessory pathway. Under normothermic cardiopulmonary bypass, the right atrium was opened and precise endocardial annular mapping was carried out. This localized the pathway just adjacent to the AV node. The accessory pathway was successfully ablated from the endocardial side, although permanent AV block also occurred, which required implantation of a pacemaker.

The other 25 patients (89.3%) underwent operation without the use of cardiopulmonary bypass. None of the patients, including those who required the endocardial approach (in whom extracorporeal circulation was established with a non-blood-primed pump), needed blood transfusions or blood products intraoperatively or postoperatively. All patients recovered rapidly, and no patient with the epicardial approach alone needed catecholamines for postoperative hemodynamic support.

Permanent AV block occurred in 1 patient (3.6%), who required a pacemaker, but there were no other major complications, eg, hemorrhage, major infection, or hepatitis. After a mean follow-up of 16.5 months (2 to 48 months), all patients remain free from tachyarrhythmias and none show preexcitation. Except for 2 patients with paroxysmal atrial fibrillation, the patients have been maintained without antiarrhythmic drugs.

Comment

At present, there are two approaches in the field of surgery for WPW syndrome. One is the endocardial approach (classic technique), developed by the pioneering work of Sealy [1], Iwa [2], and their associates. It entails extensive anatomical dissection and open heart procedures. The second is the epicardial approach, which involves minimal dissection, cryoablation, and closed heart procedures. Guiraudon and colleagues [5] reported use of an epicardial approach in 1984 in 6 patients with left free wall accessory pathways. Later they extended their technique to right free wall and posteroseptal pathways, with good results [6].

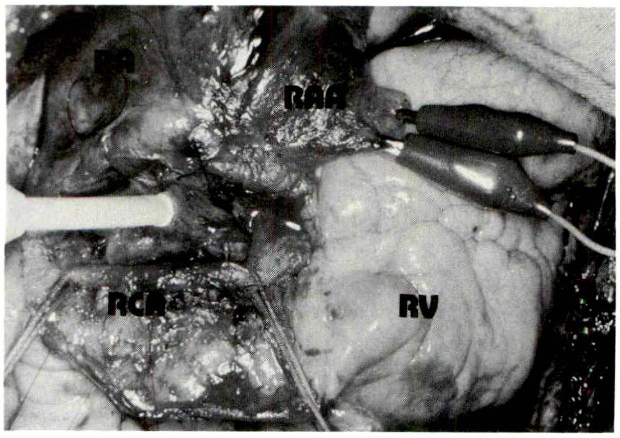

*Fig 4. Cryoablation of the right anterior accessory pathway. The atrioventricular groove fat pad of the area harboring the accessory pathway was dissected thoroughly using an ultrasonic aspirator. This area was subsequently cryoablated. The right coronary artery (*RCA*) was retracted downward so as not to be involved in the cryolesion. (*RA *= right atrium;* RAA *= right atrial appendage;* RV *= right ventricle.)*

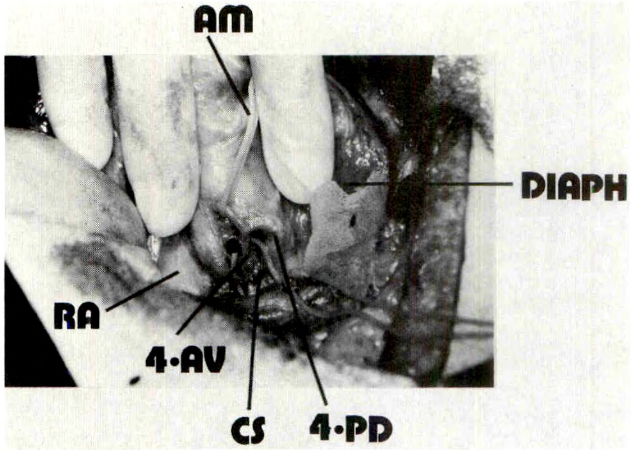

*Fig 5. Dissection of the pyramidal fat pad of the crux in a patient with a right posteroseptal accessory pathway. Operation was performed on the beating heart with the apex retracted upward without the use of heart-lung bypass. (*AM *= acute margin of right ventricle;* CS *= coronary sinus;* DIAPH *= diaphragmatic surface of right ventricle;* 4•AV *= atrioventricular node branch of right coronary artery;* 4•PD *= posterior descending branch of right coronary artery;* RA *= right atrium;* ● *= site of the accessory pathway determined by precise annular mapping.)*

In 1985, Bredikis and co-workers [10, 11] in the Soviet Union proposed a closed heart technique. For right parietal accessory pathways, their technique did not differ basically from that of Guiraudon and colleagues except that they used an ultrasonic aspirator for AV fat pad dissection, as in our closed heart technique. Septal connections and left parietal pathways were ablated by applying a cryoprobe specially designed for insertion into the coronary sinus from a small incision on the right artial wall. The probe was tightly secured by a pursestring suture.

Presently surgical treatment for patients with WPW syndrome can be given with a high success rate and a low operative risk whether it is done with the endocardial or epicardial approach.

Cox and associates [3] modified and improved the conventional endocardial approach developed by Sealy and co-workers [1] and reported their experience with 118 consecutive patients operated on in St. Louis. Kent bundles were successfully divided in all patients in their series; mortality was 5% (0.8% for patients without associated anomalies) and the incidence of complete heart block was 0.8%. Iwa and co-authors [4] presented their experience with 221 patients seen between 1973 and 1985. Their success rate was 90.0%. There were 8 deaths (3.6%), and 4.3% of the patients had complete AV block.

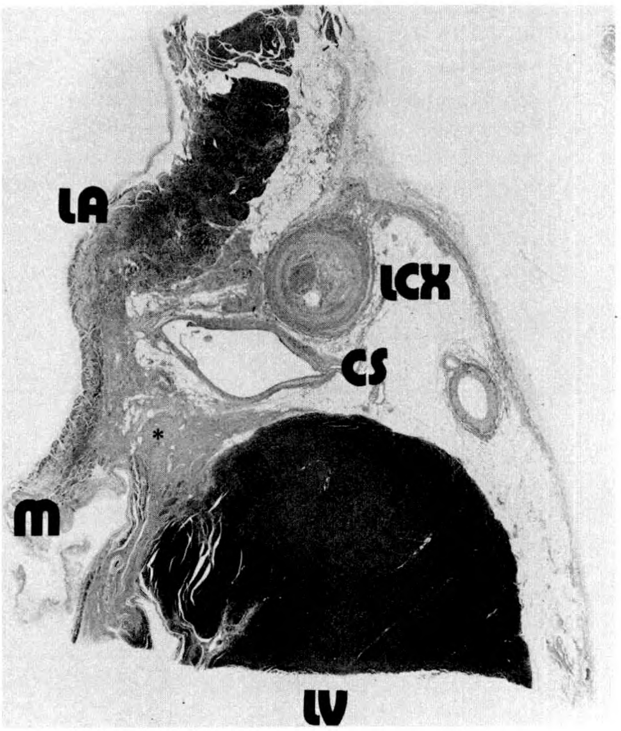

Fig 6. Low-magnification light microscope specimen of left atrioventricular junction of an adult mongrel dog. The left atrioventricular annulus of the animal had been dissected 3 months earlier and a cryoprobe at −70°C had been applied on the dissected epicardial surface for 120 seconds. Transmural thick fibrosis was formed in the annulus area (*). Also remarkable was the intimal thickening and luminal narrowing of the circumflex coronary artery (LCX), *which had been inadvertently involved in the cryolesion.* (CS = *coronary sinus;* LA = *left atrial wall;* LV = *left ventricular wall;* M = *mitral valve.) (Masson; ×10 before 38% reduction.)*

The results of Guiraudon and colleagues [6] compare favorably with those of surgeons using the endocardial open heart technique. In their series of 105 patients, Guiraudon and coauthors had no deaths and no postoperative complications. In 104 of 105 (99.0%) patients, the accessory pathways were successfully divided, although 5 patients (4.8%) required more than one operation. In 25 patients with right parietal and posteroseptal pathways operated on by Bredikis and co-workers [10], all pathways were divided. There were no deaths, and AV block did not occur.

These results show that the epicardial approach has a success rate (with few complications) equally as favorable as the conventional open heart approach. In addition, the epicardial approach has definite advantages. Because Kent bundles can be ablated without an atriotomy, this approach obviates the inherent risk and morbidity related to aortic cross-clamping and cardioplegic arrest. Continuous monitoring of conduction over the AV and accessory pathways during dissection and cryosurgery is possible even for the left parietal and posteroseptal types. This helps protect normal AV conduction and enables the surgeon to see the preexcitation disappear in the course of the procedure.

However, more than 90% of the closed heart operations of Guiraudon and associates [6] were performed with normothermic cardiopulmonary bypass to dissect and cryoablate the pathway sites in the left and posterior AV groove, because it was difficult to mobilize the AV fat pad on the vigorously beating heart using a conventional dissection technique with a scalpel without injuring major coronary vessels and the fragile atrial wall, and without causing critical hemodynamic instability while the apex was retracted upward to get better exposure. Sometimes more than 150 minutes of normothermic cardiopulmonary bypass has been necessary [6].

We used an ultrasonic aspirator (Sonotec) that allowed extensive, easy dissection of the AV fat pad without the risk of injury to the coronary vessels or the atrial wall, even when the exposure of the AV groove was limited (left free wall and posteroseptal pathways). In all 25 patients in whom the epicardial approach alone was used, extracorporeal circulation was not necessary. Hence, the majority of our patients had operation without any inherent risk or morbidity related to cardiopulmonary bypass, such as systemic heparinization, hemodilution, hemolysis, possible air embolism and thromboembolism, possible adverse effects on immunity, and influence of nonphysiological circulation on vital organs.

Validity and Precautions in Performing the Epicardial Approach

Figure 6 shows a low-magnification microscopic specimen of the left AV annulus of an adult mongrel dog. The animal was killed 3 months after cryosurgery in which a cryoprobe of −70°C was applied for 120 seconds to the annulus from the epicardial side after extensive dissection of the AV groove fat pad. Transmural dense fibrosis formed in the cryolesion, and there was no thinning of the annulus wall. This histological finding verifies that cryosurgery from the outside effectively ablates the pathway in the annulus area, at least in the chronic phase, whether it courses deep endocardially or skirts the annulus superficially.

This figure also shows a remarkable fact: the circumflex coronary artery was inadvertently involved in the cryolesion, thereby causing substantial intimal thickening with luminal narrowing. (In sharp contrast, the coronary sinus, which must have been involved in the cryolesion, does not show major luminal or mural change.) This demonstrates that, in the epicardial approach, the major coronary arteries should be retracted so as not to be involved in the cryolesion.

Bredikis and Bredikis [11] cryoablated left parietal accessory pathways with a cryoprobe inserted into the coronary sinus through a small incision in the right atrium; the probe was tightly secured with a pursestring suture. They reported that in their series of 21 pathways, 19 (90.5%) were successfully divided, although in two instances the coronary sinus wall ruptured. This necessitated coronary sinus ligation but did not cause major postoperative complications. Perhaps only an accessory pathway whose atrial insertion is located near the coronary sinus can be ablated by this technique. Our experimental results suggest that there may be a definite risk of stenosis of the coronary artery coursing along the coronary sinus in the chronic phase, especially when the coronary arterial system is of the left dominant type (see Fig 6).

Potential Limitations of Epicardial Approach

In 3 (10.7%) of our 28 patients, the pathway necessitated an additional ablative procedure from the endocardial side for successful division. In 1 patient, this was due to a technical failure when the bar of the ultrasonic aspirator inadvertently tore the left atrial wall. This does not constitute a limitation of the epicardial approach because it can be readily overcome by improving technical skill and by modifying the tip of the bar so that it angles slightly (approximately 30 degrees). This would allow it to be applied easily to the left and posteroseptal AV groove through a narrow operative field.

In 1 patient with bilateral Kent bundles, the left pathway could not be cryoablated with a temperature of −60°C from the outside. A precise annular map of the dissected AV groove showed that the arrival of the impulse at the point of earliest excitation preceded the onset of the delta wave of the limb-lead electrocardiogram by only 31 ms. In patients in whom the epicardial approach alone could divide the pathway, the earliest surface point excited more than 60 ms earlier than the onset of the delta wave. From this, we assumed that in this patient, the accessory pathway was situated deep on the endocardial side of the AV junction and was continuously warmed by the blood inside the cardiac chamber, while the cryosurgery was carried out from the outside.

Initially the cryoprobe temperature of around −70°C was chosen following the cryosurgical experience reported by Gallagher and colleagues [12]. (They chose −70°C because it was the maximum temperature attained with their instrument, which utilized nitrous oxide as a coolant.) Our experimental results (see Fig 6) indicate that with −70°C cryosurgery of the annulus for 120 seconds from the epicardial side, transmural thick fibrosis is formed in the chronic phase. Theoretically the Kent bundle in any depth within the AV junction can be ablated in the long run. However, the cryosurgical experience of Gallagher and co-workers was with the classic endocardial approach in which the cryoprobe was applied from the inside with cardiopulmonary bypass; there was no blood inside the cavity to warm the cryolesion. With the temperature around −70°C, cryosurgery may fail to destroy the accessory pathway, at least in the immediate postoperative period.

Our cryosurgical instrument uses liquid nitrogen as a coolant, and a maximum temperature of −190°C can be attained. Our recent experiments involving mongrel canine hearts (unpublished data) showed that a cryolesion formed in the AV annulus by applying a probe colder than −150°C for two minutes was significantly larger and deeper than a cryolesion formed by a probe of −60°C applied for the same duration. Based on this finding, we have lowered the temperature of the cryoprobe to −150°C in the clinical setting. We applied this strategy in the last 7 patients, and had excellent results and no complications. Whether this use of extremely low-temperature cryosurgery can overcome the difficulty of successfully cryoablating pathways deep in the endocardial side with the epicardial approach awaits further experience.

Precise epicardial mapping and extensive dissection are prerequisites for successful ablation, and the operation must fail, however cold the temperature, if the area determined by the mapping is inaccurate or the dissection is incomplete. In fact, 3 patients required reoperation probably because of incomplete dissection of the accessory pathway sites. We know the sites were accurately located by intraoperative mapping because in the second operation, the same sites were extensively dissected, and subsequent cryosurgery from the outside divided the pathways permanently.

Another patient who required the endocardial approach had a right posteroseptal pathway. As Guiraudon and associates [13] reported, the posteroseptal annulus can be approached from the outside. In 6 of our 7 patients with posteroseptal pathways, the pyramidal fat pad filling the paraseptal space was dissected with the heart retracted upside down, and cryosurgery on the earliest excitation point in the paraseptal annulus area successfully divided the pathway without the use of cardiopulmonary bypass. In all of these successful procedures, the pathway was near or outside the ostium of the coronary sinus. However, in the patient in whom we failed to accomplish ablation by the epicardial approach, the earliest excitation point was located deeply inward from the os of the coronary sinus. Endocardial mapping after atriotomy revealed the pathway to be located just adjacent to the AV node, approximately 20 mm anterior to the os of the coronary sinus. The pathway was divided by cryoablation from the inside, although complete AV block occurred simultaneously.

An accessory pathway located in the septal area anterior to the ostium of the coronary sinus might be inaccessible even with extensive dissection from the epicardial side. Consequently this location might constitute a limitation of the epicardial approach. We have now excluded this location of the Kent bundle (septal pathway anterior to the os of the coronary sinus and just adjacent to the AV node) from our indications for the epicardial approach.

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Significance of Extramucosal Residual Tumor at the Bronchial Resection Margin

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Extramucosal microscopic residual disease (MRD) at the bronchial resection margin was identified in 45 (1.6%) of 2,890 patients who underwent resection of primary non–small cell lung cancer between 1975 and 1985. In 9 of these patients, residual tumor was confined to submucosal lymphatics, whereas in the other 36, MRD was found in peribronchial soft tissue. All patients underwent complete mediastinal lymphadenectomy. Three patients had stage I disease, 3 had stage II, 33 had stage IIIa, 4 had stage IIIb, and 2 had stage IV. Recurrent disease developed in 34 (81%) of the evaluable patients; the recurrence was local in 11 (32%). Median time from operation to diagnosis of local recurrence was 8 months. Sixty percent of the recurrences in the N0 group were local, and only 23% of those in the N2 group were local. Extramucosal MRD is most frequently associated with advanced-stage disease. Postoperative therapy had no effect on the development of recurrent disease. We found no difference in survival between patients whose initial site of recurrence was local as opposed to distant. Median survival after the identification of either local or distant recurrence was 5 months. The finding of extramucosal MRD identifies a subset of patients with a poorer prognosis compared with those with clear resection margins.

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Definitive surgical treatment of non–small cell lung cancer mandates complete resection of the primary tumor in combination with mediastinal lymphadenectomy for staging. Incomplete resections can result from the inability to remove all gross disease or can become apparent later when microscopic residual disease (MRD) is identified at the resection margin. The pulmonary vessels are infrequently the site of MRD. The bronchus, however, can contain MRD as a result of direct mucosal extension from endobronchial tumor or extramucosal involvement of peribronchial lymphatics or soft tissue [1–4].

Some reports [2, 4, 5] addressing the importance of MRD at the bronchial resection margin grouped these two types of residual tumor involvement together. However, Soorae and Stevenson [3] proposed that the two patterns are biologically distinct in their clinical behavior, and suggested that residual tumor in the peribronchial tissue had a greater propensity for lymphatic spread. These studies are difficult to interpret because of incomplete surgical staging.

Because of the presumed distinct clinical and pathological behavior of extramucosal as opposed to mucosal residual disease, we decided to look at a group of patients with only extramucosal residual disease documented at the bronchial resection margin. Intraoperative frozen section of the bronchial resection margin can be expected to reveal mucosal involvement with residual disease, but extramucosal involvement can be overlooked or, even if noted by the pathologist, ignored by the surgeon. To accurately assess the natural history and prognostic implications, we conducted a retrospective review of completely staged patients with non–small cell lung cancer and extramucosal MRD at the bronchial resection margin. All patients underwent complete mediastinal lymphadenectomy, and thus the intraoperative staging is particularly accurate.

Material and Methods

The charts of all patients who had pulmonary resection for primary non–small cell lung cancer at Memorial Sloan-Kettering Cancer Center during the 11-year period 1975 through 1985 were reviewed. Details of clinical presentation, tumor location, histology, lymph node involvement, extent of surgical resection, operative morbidity and mortality, adjuvant therapy, and recurrence and survival data were recorded for each patient. All patients underwent complete mediastinal lymphadenectomy. Staging is reported according to the recent modification of the TNM classification for lung cancer [6].

Follow-up data were derived from hospital or office charts and telephone calls to referring physicians or patient's families when necessary. Follow-up was 98% complete, with only 1 patient lost to follow-up. Recurrent disease was determined to be local or distant. Local recurrence was defined as tumor recurring within the ipsilateral lung, bronchial stump, or hemithorax. Distant recurrences were those that occurred outside the ipsilateral hemithorax.

Survival was analyzed by the product limit method of Kaplan and Meier [7], and curves were compared using the log-rank test (Mantel-Haenszel) [8].

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Results

Extramucosal MRD was present in 1.6% (45/2,890) of patients who underwent resection of non–small cell lung cancer during the study interval. Nine of these patients had tumor confined to submucosal lymphatics without mucosal involvement, and the other 36 had tumor in peribronchial soft tissue. There were 32 men and 13 women ranging in age from 38 to 77 years with a mean age of 57.7 years. Cough, the most common presenting complaint, was found in 14 (31%). Ten patients (22%) noted either chest pain or hemoptysis. The average duration of symptoms was 3.9 months (range, 1 to 36 months). One third of the patients were asymptomatic at presentation.

Upper lobe lesions accounted for the majority (67%) of primary tumors, as expected. On the right side, there were 16 (35.6%) upper lobe, 3 (6.7%) middle lobe, and 3 (6.7%) lower lobe lesions. There were 14 (31.1%) left upper lobe lesions and 9 (20.0%) left lower lobe lesions. Adenocarcinoma was the predominant histological finding (26 patients, 57.8%). Fifteen patients (33.3%) had squamous cell carcinoma, 2 (4.4%) had large cell carcinoma, and 2 had bronchioloalveolar carcinoma. Twenty patients had endobronchial lesions noted on bronchoscopic examination.

Twenty-nine patients (64.4%) underwent lobectomy, 11 (24.4%) had pneumonectomy, and 5 (11.1%) underwent bilobectomy. Sleeve resection of the main bronchus was carried out in 3 patients undergoing lobectomy or bilobectomy, and sleeve resection of the trachea was done in 1 patient having pneumonectomy. In 37 patients (82.2%) the resection was considered complete, and in the remaining 8 patients, it was the opinion of the surgeon that the resection was incomplete. No "incomplete" resection was judged to be so because of gross residual disease in peribronchial tissue.

Only 6 patients had other than stage III disease: 3 with stage I and 3 with stage II disease. Thirty-seven patients had stage III disease: 33 had stage IIIa and 4, stage IIIb. Two patients with stage IV disease also underwent resection. Intraoperative frozen section of the bronchial resection margin was done in all except 9 patients. In the other 36 patients, all of whom were, of course, subsequently found to have extramucosal MRD, fifteen (41.7%) of the frozen sections failed to show tumor at the resection margin.

Morbidity and Mortality

Three patients (6.7%) died in the immediate postoperative period. One of them, a 54-year-old man, had a massive intrathoracic bleed after the chest was closed but while he was still in the operating room. Despite immediate reentry and control of the hemorrhage, he could not be resuscitated. The second death was that of a 43-year-old woman who died of extensive bronchopneumonia on the ninth postoperative day. The third patient had been discharged from Memorial Hospital and was admitted urgently to an outside hospital on the 28th postoperative day. No autopsy was done, and we are uncertain as to the exact cause of death.

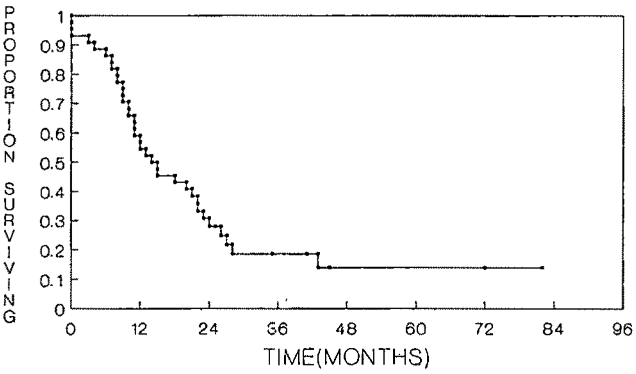

Fig 1. Overall survival from time of operation for the entire group.

Among the 42 operative survivors, one or more complications were seen in 21 patients (50%). The most frequent complications were pneumonia (7 patients, 33.3%) and prolonged air leaks (5 patients, 23.8%). The mean duration of air leak was 14 days (range, nine to 18 days). There were three recurrent laryngeal nerve injuries (14.3%), two major cardiac arrhythmias (9.5%), two wound infections, and two deep venous thromboses.

Postoperative Therapy

Thirty-three patients received some form of additional treatment after operation. Radiation therapy was administered to 26 patients, chemotherapy to 2, and combined radiation therapy and chemotherapy to 5 patients. Total radiation doses ranged from 300 to 520 cGy.

Survival

Median survival for the entire group was 15 months with actuarial survival of 60%, 33%, and 20% at 12, 24, and 36 months, respectively (Fig 1). Of the 42 operative survivors, 4 are alive with disease at 20 to 72 months following treatment. Five patients are free of disease at 23 to 81 months, but 2 of them have been treated for recurrent disease. Twenty-eight (67%) have died as a result of lung cancer, and 4 others died of causes not directly attributable to their disease. The probability of survival could not be correlated with histology (Fig 2), although there was a trend toward improved survival with squamous cell car-

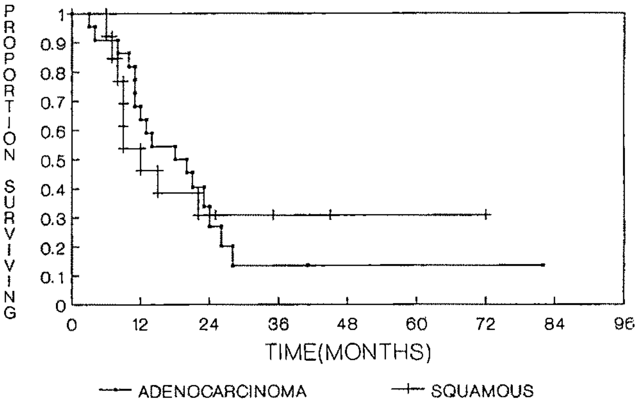

Fig 2. Survival by histology (p = not significant).

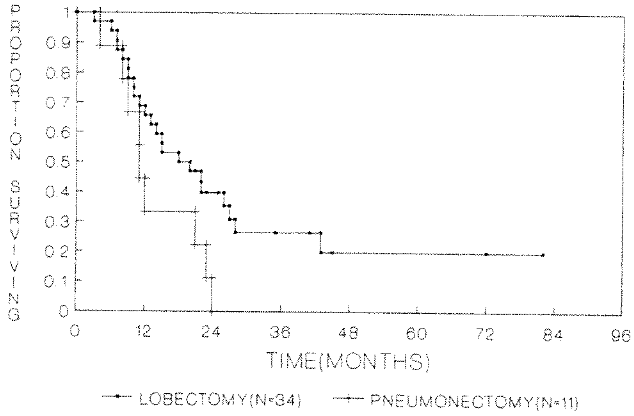

Fig 3. Survival by operative procedure ($\chi^2 = 3.96$, $p < 0.05$).

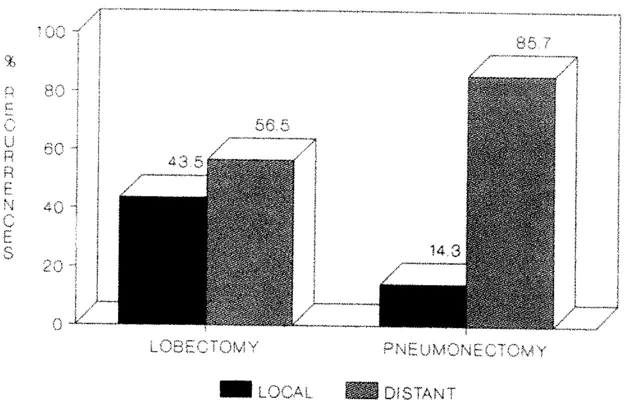

Fig 5. Type of recurrence by operative procedures.

cinoma. Survival, however, was significantly better ($\chi^2 = 3.96$, $p < 0.05$) in those patients who underwent lobectomy (Fig 3).

Recurrence

Recurrent disease developed in 34 (81%) of the evaluable patients, and details of the nature of the recurrence are known for 31. There were 11 local recurrences (32%). Eight were detected bronchoscopically in the bronchial stump or adjacent bronchial mucosa. Median time from operation to diagnosis of local recurrence was 8 months. Eight of the 11 recurrences were identified within the first year after operation.

Twenty patients had distant disease as the first manifestation of metastatic tumor. In 7 patients, brain metastases developed as the first site of distant disease. Seventeen of the 20 patients had distant disease within the first year after operation, and the median interval from resection to first recurrence was 8 months.

Figure 4 summarizes the recurrence data according to nodal status. Recurrent tumor developed in 56% (5/9) of the N0 patients, 90% (9/10) of those with N1 disease, and 78% (18/23) with N2 disease. Sixty percent of the recurrences in the N0 group were local, whereas only 23% of those in the N2 group were local. There were fewer local recurrences in the group of patients who had pneumonectomy compared with those who had lobectomy or bilobectomy (Fig 5). Locally recurrent disease accounted for 40% of recurrences in patients with squamous cell carcinoma but only 28% in patients with adenocarcinoma.

Thirty-three (79%) of 42 patients who survived operation received postoperative radiation therapy or chemotherapy alone or in combination. Of the 11 patients with local recurrence, 9 had received postoperative irradiation. Recurrent disease developed in 7 of these 9 within 1 year of operation. The remaining 2 patients had recurrence at 13 months and 22 months. All 9 patients died of disease within 1 year of the diagnosis of recurrent disease (median time, 5 months). The 2 other patients with local recurrence remain alive, 1 with disease 68 months after recurrence and the other with no evidence of disease 6 months after completion pneumonectomy. Neither of these patients received postoperative adjuvant treatment.

Despite treatment, once recurrent disease was diagnosed, survival was poor (Fig 6). Median survival after the identification of either local or distant recurrence was 5 months. Eighty percent of those with a local recurrence and 70% of those with distant disease were dead within 1 year of the diagnosis of recurrence. One patient who had recurrence in the bronchial stump 42 months after operation underwent a completion pneumonectomy and has remained free of disease for 6 months. Another patient showed recurrence in the bronchus less than 4 months

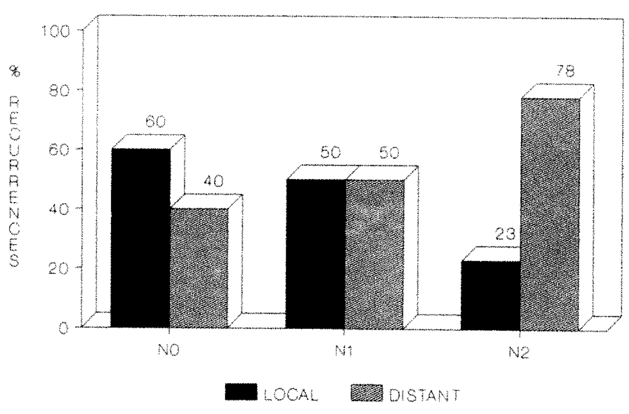

Fig 4. Type of recurrence based on nodal (N) status.

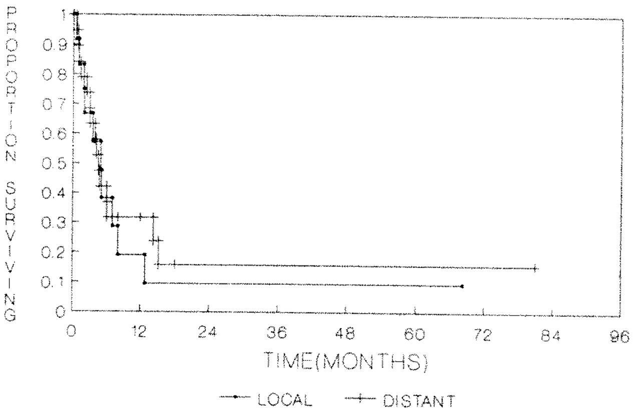

Fig 6. Survival from time of diagnosis of recurrent disease (p = not significant).

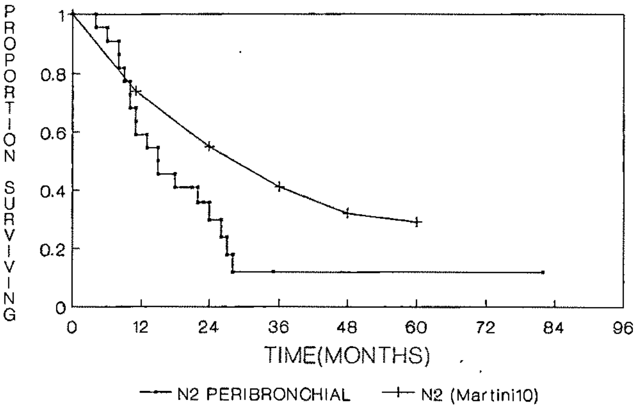

Fig 7. Survival of N2 patients with extramucosal microscopic residual disease compared with a group of N2 patients with no residual disease.

after operation, but is alive and well 68 months after the recurrence was documented. A third patient who was found to have a malignant pleural effusion 2 months after operation remains free of disease 81 months after chemotherapy.

Comment

The problem of residual tumor at the bronchial resection margin was addressed, although indirectly, by Habein and associates [9] in 1956. In 1974, Shields [1] differentiated between various types of residual disease at the bronchial stump. In a report detailing the outcome for patients entered on protocols of the Veterans Administration Surgical Adjuvant Group, he noted that patients with gross tumor remaining at the bronchial margin had the same poor prognosis as those with residual mediastinal lymph node disease. However, those patients who had a grossly normal bronchial stump but were found to have MRD lived longer than patients with any other category of residual disease. Shields further characterized the microscopic residual as peribronchial involvement or submucosal involvement.

Soorae and Stevenson [3] described four patterns of MRD at the bronchial margin: direct extension of the main tumor mass proximally in the bronchial wall, lymphatic permeation, involvement of peribronchial tissue by clumps of cells separate from the main tumor mass, and carcinoma in situ. In all categories, an adverse effect on patient survival was observed.

The incidence of extramucosal MRD in the present series was 1.6%. This is in line with data from other published reports [1, 3, 4]. Thirty-three patients (73%) in the present series had pathological stage IIIa disease, 24 classified on the basis of mediastinal lymph node involvement. Survival in this group of N2 patients was considerably worse at 2 years compared with another group of N2 patients with complete resection and without MRD operated on at the same institution during approximately the same period (Fig 7) [10]. This comparison is made for illustrative purposes, and the lack of statistical validity is recognized. It is only the rare patient with extramucosal MRD who has pathological stage I or stage II disease.

Fifty percent of our patients sustained one or more perioperative complications, admittedly a high percentage. We have no specific explanation as to why the incidence is so high in this small group of patients. None of the complications appeared to be specifically related to the presence of extramucosal MRD. Soorae and Stevenson [3], in a series comprised mainly of patients with mucosal MRD, reported a 12.5% incidence of bronchopleural fistula. Heikkila and colleagues [4] noted this complication in 13.6% of patients, although again the majority of their patients had mucosal MRD. The lack of bronchopleural fistulas in our study could be explained by our decision to look at only patients with extramucosal MRD at the bronchial resection margin.

Prolonged survival with documented MRD at the bronchial resection margin has been reported [1, 2]. Soorae and Stevenson [3] had only a single 5-year survivor among 20 patients with extramucosal MRD. The lack of complete staging and variable postoperative therapy makes comparison with other studies difficult. Our 5-year survival of less than 20% is undoubtedly due more to the fact that all but 6 of our patients had stage III or greater disease than solely to the presence of a positive margin.

The problem of MRD at the bronchial resection margin might be more prevalent than is currently appreciated. Two recent studies involving stage I and stage II patients present some intriguing findings. The Ludwig Lung Cancer Study Group [11] found the bronchial resection margin to be the single most frequent site of recurrence, constituting 16% of all recurrences, local or distant. This represented 40% of their intrathoracic failures. Patients who had undergone pneumonectomy or bilobectomy had fewer initial intrathoracic failures than patients in whom lobectomy was performed. The authors correctly concluded that "more emphasis should be given to local control." Iascone and co-workers [12] noted a 21% incidence of local recurrence (including nodal recurrences) in a series of 95 patients. Local recurrence accounted for 75% of recurrences in patients with N0 disease and 29% in patients with N1 disease. The authors thought that a more extensive procedure, ie, pneumonectomy, could have potentially been "curative" in many of these N0 and N1 patients. However, an alternative explanation would be that these patients were "understaged" at operation because of the failure to carry out adequate lymph node dissection. This could account for the high incidence of local recurrence and limited survival.

Because of our practice of routinely performing mediastinal lymphadenectomy, we can say with confidence that our data demonstrate that extramucosal MRD is most frequently associated with advanced-stage disease, as 82% of the patients in our series had stage III disease. Thus, a more aggressive surgical procedure alone would seem unlikely to influence survival because the majority of patients first have recurrence with, and subsequently die of, distant disease. However, we found no difference in survival between patients who had local disease as opposed to distant disease as the initial site of recurrence, and therefore we must consider whether in certain stage III patients a more extensive resection might have been associated with longer survival. The problem, of course, is that we currently have no way of selecting these patients. Certainly one should be very aggressive about documenting and excising any extramucosal MRD at the time of operation. A more radical surgical approach to eliminate extramucosal MRD would be expected to benefit patients with stage I or stage II disease.

Frozen-section analysis of the bronchial resection margin usually reveals mucosal MRD if present, but can miss extramucosal disease. Separate specimens of suspicious peribronchial soft tissue that remains in situ may have to be sent for frozen-section analysis. A frozen-section diagnosis of tumor in peribronchial soft tissue should not be ignored. Intraoperative identification of MRD permits resection of additional bronchus or lung tissue. If extramucosal MRD is identified only by permanent histological section, one might consider reoperation with further resection for those patients known to have N0 or N1 disease proven by complete mediastinal and hilar lymphadenectomy performed at the original procedure. This further underscores the importance of the information to be gained from and the potential therapeutic importance of a mediastinal lymph node dissection as opposed to lymph node sampling.

It would be difficult to make a case for reoperation to remove further local disease in patients with documented N2 disease. Rather than routinely proceeding with pneumonectomy, when appropriate we favor a sleeve resection, which carries a lower incidence of morbidity and mortality and has comparable long-term results [13, 14]. Extending the magnitude of the resection is unlikely to alter the outcome in patients with N2 disease, but certainly initial efforts should be directed toward removing all gross disease. The prevention of local recurrence remains preferable to other current treatment options.

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Delayed Primary Closure After Sternal Wound Infection

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Infected median sternotomy is a major complication of cardiac operations. Over a 30-month period, 25 sternal wound infections were treated at a single institution. Twenty-four (2.7%) followed 883 operations with cardiopulmonary bypass, and 1 followed median sternotomy for a noncardiac procedure. Twenty-one of the 25 patients survived to sternal closure. Eighteen patients were treated with delayed primary closure and 3 with pectoralis muscle flaps. Fifteen patients (83%) had an uneventful postoperative course after delayed primary closure. In 2 patients reoperation was required for sternal dehiscence, and in 1 patient a superficial wound infection developed, which was treated with local wound care. In all 18 patients the sternum eventually healed. Criteria for delayed primary closure included clean tissue surfaces without purulent debris, the absence of pockets of purulent drainage, and negative wound cultures obtained 24 hours before closure. The average time from operation to sternal incision and drainage was 11 days (range, five to 59 days). Delayed primary closure was performed nine days after incision and drainage (range, five to 27 days). The average hospital stay was 24 days after sternal incision and drainage (range, nine to 85 days). Cultures from specimens taken at the time of sternal incision and drainage were positive in all patients. Wound cultures were positive at the time of sternal closure in 5 patients. Wound complications developed in 2 of these 5 patients. Delayed primary closure has many of the advantages of classic methods, but fewer complications. Results are comparable, while allowing simpler wound care and less cosmetic deformity. Delayed primary closure is an acceptable alternative in the treatment of sternal wound infections.

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Despite advances in surgical technique and antimicrobial therapy, median sternotomy incisions remain at risk for infection. Infected median sternotomy represents a major complication of cardiac operations. Many methods have been introduced to treat this problem. This study details our experience in the management of this challenging problem and compares our results with historical data.

Material and Methods

During a 30-month period ending June 1987, 883 patients underwent cardiac operation at Gundersen/Lutheran Medical Center. Standard methods of skin preparation and wound closure were employed. A ten-minute skin preparation performed with povidone-iodine solution was used for all patients. Paper drapes were placed, and all exposed skin was completely covered with adhesive plastic drapes. At the termination of the procedure, the sternum was reapproximated with No. 5 stainless steel wire, the subcutaneous tissue was approximated with 2-0 polydioxanone suture, and the skin was closed with a running subcuticular stitch of 4-0 undyed polyglycolic acid suture. One dose of vancomycin was administered intravenously routinely before operation, and two additional doses were administered after the procedure.

Postoperatively, wounds were examined on a daily basis by the attending surgeon. If purulent material was observed in a sternal wound, a small opening was made in the skin. If the deeper layers indicated the presence of infection (ie, exposed sternal wire or purulent drainage coming from behind the sternum), a major sternal infection was diagnosed. The entire wound was then opened under general anesthesia. All suture material was removed, specimens were obtained for culture, and any loose debris was removed. Vancomycin, often in association with a third-generation cephalosporin (50%), was administered before the incision was made and drainage begun. This regimen was continued until culture results were obtained; the choice of subsequent antibiotics was based on bacterial sensitivity. Cotton gauze dressings were placed in contact with all wound surfaces, and the incision was left open. Four to six hours after incision and drainage, the dressing was first changed. The gauze was removed, and fresh gauze was placed in contact with all surfaces. If the wound was saturated with purulent material or serous fluid, the gauze was placed into the wound dry. When the surfaces became dry and nonpurulent, cotton gauze moistened with normal saline solution was used. Dressing changes were performed every four hours at the bedside using a clean, but not rigidly sterile technique.

Criteria for delayed primary closure included clean

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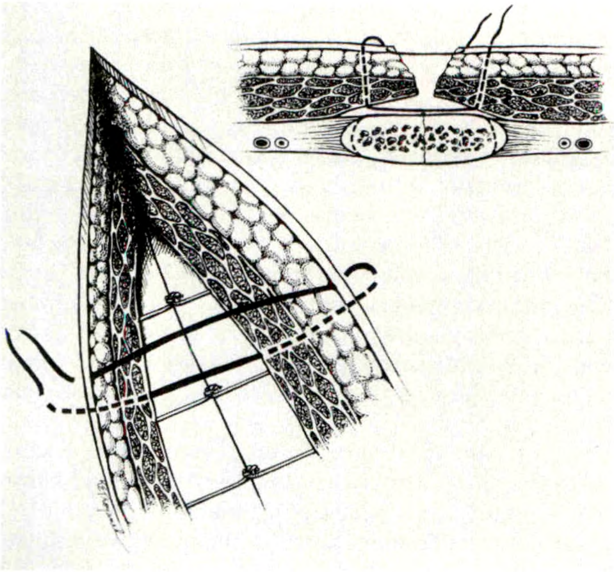

Fig 1. Delayed primary closure of sternum depicting dissection over sternum, allowing for midline closure.

tissue surfaces without purulent debris and preferably healthy granulation tissue, the absence of pockets of purulent drainage, and a negative wound culture obtained 24 hours before closure. When these criteria were fulfilled, the patient was returned to the operating room. Further debridement was carried out with excision of only obviously devitalized tissue. Granulation tissue on the cut surfaces of the sternum was debrided to enable bone-to-bone apposition. Multiple No. 5 stainless steel wires were placed 1 to 2 cm apart between the two sides of the sternum. These wires were placed either through or around the sternum. The sternum was then closed tightly. If space remained beneath the sternum, large silicone drains (Axiom, Paramount, CA) were placed and brought out through the epigastric skin. Dissection in a plane just over the sternum with undermining of 2 to 3 cm of tissue allowed for midline skin closure. The subcutaneous tissue and skin were closed as a single layer using interrupted vertical mattress 1-0 polypropylene sutures with good apposition of all tissue layers (Fig 1). Additional skin sutures were usually not necessary and were used only when skin apposition was inadequate.

Hospital charts and outpatient records were reviewed for each patient. Times from initial operation to incision and drainage, incision and drainage to delayed primary closure, and delayed primary closure to discharge were noted. Culture results and antibiotic therapy at the time of incision and drainage and before closure were recorded. Potential predisposing factors to sternal wound infection were investigated, and included postoperative bleeding, sternal dehiscence, history of diabetes mellitus, and preoperative corticosteroid therapy.

Statistical comparison of results between groups was made using χ^2 analysis of two proportions with Yates' correction. Level of confidence was defined at a p value of less than 0.05.

Results

Between January 1985 and June 1987, 883 patients underwent cardiac procedures at Gundersen/Lutheran Medical Center. Ninety-three patients (11%) had a previous sternotomy for a cardiac procedure. Median sternotomy was performed in 87 patients for procedures other than coronary artery bypass grafting (CABG) or valve replacement. Coronary artery bypass grafting was performed in 579 patients, and internal mammary artery grafts were used in 458 (79%) of them. One hundred twenty-four patients underwent valve replacement, either alone or in combination with CABG.

During the two and a half–year study period, a sternal wound infection developed in 25 patients, 24 of whom had undergone cardiopulmonary bypass (Table 1). In the remaining patient, a sternal infection occurred after median sternotomy for thymectomy. There were 16 men (64%), and age ranged from 25 to 80 years (mean age, 62 years). Sternal wound infection developed in 6 (2.4%) of 248 patients undergoing CABG with a single internal mammary artery and 7 (3.3%) of 210 patients with bilateral internal mammary artery grafts. Three sternal infections (2.5%) occurred in 121 patients after CABG with vein grafts alone. There were no significant differences between these groups. Four infections (5.1%) occurred in 78 patients undergoing a valve operation. There were no wound infections in 46 patients undergoing a combination of valve replacement and CABG. Four (4.3%) of 93 patients with sternal infections had had a previous sternotomy.

Sternal wound infections occurred most commonly within 2 weeks of median sternotomy (mean time, 11 days), with a range of five to 59 days. Organisms included *Staphylococcus aureus* in 12 patients, *Staphylococcus epidermidis* in 6, *Enterobacter* species in 4, *Escherichia coli* in 3, and miscellaneous gram-negative bacteria in 5. Cultures from two wounds grew anaerobic organisms, and cultures from seven wounds grew multiple organisms. Blood cultures from 11 individuals grew organisms identical to wound cultures.

Table 1. Incidence of Sternal Infection After Cardiopulmonary Bypass

Operation	No. of Patients	No. of Sternal Infections[a]
Myocardial revascularization	579	16
Vein graft	121	3 (2.5)
Internal mammary artery	458	13 (2.8)
Unilateral	248	6 (2.4)
Bilateral	210	7 (3.3)
Valve replacement	78	4 (5.1)
Combination valve and CABG	46	0 (0)
Repeat sternotomy	93	4 (4.3)
Other	87	0 (0)
Total	883	24 (2.7)

[a] Numbers in parentheses are percentages.

CABG = coronary artery bypass grafting.

Four patients (16%) with sternal infection died 11 to 42 days after operation. Three died of complications unrelated to sternal wound infection. One patient sustained a stroke after double-valve replacement. Severe congestive heart failure, renal failure, and arrhythmias developed in another patient after mitral valve replacement. The third patient sustained a fatal perioperative myocardial infarction after a second CABG. One patient (4%) with steroid-dependent rheumatoid arthritis died on the 17th postoperative day of unrelenting sepsis related to the sternal infection.

Twenty-one patients survived to sternal closure. Delayed primary closure was used for 18 patients. The mean time to delayed primary closure was nine days after incision and drainage (range, five to 27 days). Cultures grown from specimens taken 24 hours before closure were positive in 5 of the 18 patients. For these 5 patients, the cultures were initially reported to be negative before operation, but subsequently were positive for bacteria. Fifteen patients had an uneventful postoperative course. Two patients required reoperation at a later date for sternal dehiscence. Neither patient had evidence of infection at the time of reclosure. A superficial wound infection, which was treated with local wound care, developed in another patient. Two of 5 patients with delayed positive wound cultures had sternal wound complications versus 1 of 13 patients with negative cultures ($p = 0.17$).

Pectoralis muscle flaps were used successfully to close the sternal wound in the other 3 patients. The sternum in each of these 3 patients had become necrotic and would not have held sutures. Hospital stay after delayed primary closure was 14 days (range, four to 73 days). Total hospitalization from incision and drainage to discharge was 24 days (range, nine to 85 days).

Comment

Median sternotomy has become the incision of choice for the majority of open cardiac procedures since it was proposed by Julian and colleagues [1] in 1957. Sternal infection after median sternotomy is an uncommon complication with an incidence ranging from 0.4% to 5.0% [2–6]. A wide range of treatment methods has evolved for mediastinal infection after median sternotomy.

Two approaches to surgical management of sternal wound infections have been widely used. The "open" method involves debridement and open packing of the sternum with healing by secondary intention. This has later been modified with the option of secondary closure using a variety of flaps, including omental, pectoralis, latissimus dorsi, and rectus abdominis [7–11]. The advantage of the open method is removal of potentially undrained areas of infection while active debridement continues with dressing changes. Hospitalization has been prolonged, with complete healing reported to take as long as 16 months [12]. This, however, has now been greatly reduced with the use of myocutaneous flap coverage [7–11]. Mortality with the open technique has ranged from 20% to 45% [12, 13]. The potentially disastrous complication of hemorrhage from exposed mediastinal vessels is present until closure is complete [6, 14]. In addition, the lack of sternal union can severely impair respiratory function [5] and cause substantial cosmetic deformity.

Schumacker and Mandelbaum [15] in 1963 reported results in 5 patients treated using a "closed" method. Treatment was by sternal debridement with closure of the sternotomy over infusion catheters and two or more large drainage catheters. The subcutaneous tissue was left open and allowed to heal by secondary intention [3, 14] or was closed primarily with or without drainage [2, 5, 16, 17]. Postoperatively, the mediastinum was irrigated with a wide variety of preparations, including antibiotic and povidone-iodine solution [2, 3, 14, 16–19]. The largest advantage to the irrigation method was a shortened length of hospitalization. Jimenez-Martinez and associates [5] reported discharge of all patients in less than 30 days, and Grossi and co-workers [20] reported a mean hospital stay of 43 days after sternal closure over the irrigating catheter system. Sternal closure returned stability to the thoracic cavity and improved pulmonary function. Cosmetic results have also been more pleasing.

Several complications of this technique have been reported. Sternal wounds closed with the irrigation method can create a potentially undrained cavity. Reexploration for a loculate infection has been required in 13% to 66% of patients [2, 6]. Mediastinal catheters have become occluded, with seepage of irrigation solution through the incision, creating management difficulties. Mediastinal catheters have eroded through adjacent tissues, and this has resulted in life-threatening hemorrhage [14]. Antibiotic solutions can also predispose to superinfections [1–3], and systemic toxicity of the irrigation solution has been reported [2, 6, 18].

Many factors in the perioperative period have been shown to predispose sternal incisions to infection. The incidence of mediastinal infection has been documented to be greater when the internal mammary artery was used for coronary revascularization [12, 21]. Culliford and colleagues [16] reported an infection rate of 1.1% in patients undergoing coronary revascularization with saphenous vein grafts. The rate of sternal infection rose to 2.3% when coronary revascularization with a single internal mammary artery graft was used and to 8.5% if both internal mammary arteries were used. The higher incidence of sternal wound infection associated with internal mammary artery grafts has been attributed to increased hemorrhage and longer duration of the procedure [12].

In the series of Culliford and co-workers [16], 42% of patients with sternal wound infections required reexploration, most for postoperative bleeding. In our series, reexploration was necessary in 48% of patients, 16% for sternal dehiscence and 32% for postoperative bleeding. Arnold [21] demonstrated a relationship between dissection and sternal ischemia. With the use of dye injection in cadavers before and after mobilization, tributaries of the internal mammary artery were demonstrated from the anterior and posterior periosteal plexuses which constitute the primary blood supply to the sternum. Arnold proposed that sternal ischemia after internal mammary artery dissection leads to impaired healing and potential sternal wound dehiscence with infection. In our study, there was no significant difference in the infection rate when the types of conduits used for bypass were compared.

The most common organism cultured in our series was

S aureus. This has been the most common pathogen reported in the vast majority of studies [3, 5, 13, 16, 20]. *Staphylococcus epidermidis* was grown from the specimens from 6 patients. The incidence of *S epidermidis* as the primary pathogen is increasing because of the routine use of perioperative antistaphylococcal, penicillinase-resistant antibiotics [2, 16]. In large centers, up to 30% of *S epidermidis* isolates have become resistant to many antibiotics [2]. Engelman and associates [2] reported 35% of sternal infections involved *S epidermidis*, and Culliford and coauthors [16] reported involvement of more than half of sternal infections with *S epidermidis*. Gram-negative organisms have been commonly isolated, whereas mixed infections have been found in up to 40% of patients [2, 3, 13, 16]. For 2 patients in our series, cultures grew anaerobic organisms, one as the sole organism (*Bacteroides fragilis*) and the other (*Peptostreptococcus*) in conjunction with an aerobic gram-negative organism. Anaerobic infections have been only rarely implicated in other series [14, 22].

Delayed primary closure has many advantages of previously described methods, while avoiding several of their shortcomings. Initially, sternal wounds are treated in an open fashion, which eliminates potentially undrained spaces and allows for active debridement with dressing changes. The complication of hemorrhage from mediastinal vessels is minimized by the shorter period before closure, and was not seen in this study. This method also avoids complications secondary to indwelling mediastinal irrigation catheters and problems associated with irrigation solutions.

Hospitalization averaged 24 days from the time of incision and drainage, and nine days from the time of delayed primary closure. These results are comparable with reports in the literature using either the closed or open method [5, 7, 11–13, 20]. With delayed primary closure, 2 (11%) of 18 patients required reoperation at later dates for sternal dehiscence; however, neither had evidence of infection at the time of reclosure. Fifteen (83%) of the 18 patients healed without incident. All 18 sternal wounds eventually healed with acceptable cosmetic results, including no visible chest wall deformity.

In conclusion, delayed primary closure is a method of treatment for sternal wound infection that has evolved from both the closed and open methods. Criteria for closure include absence of purulent drainage, clean tissue surfaces, and negative wound cultures before closure. Delayed primary closure of sternal wound infection is an acceptable method of treatment with excellent cosmetic results.

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Neonatal Pneumopericardium With High-Frequency Ventilation

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Pneumopericardium is an uncommon condition in the neonate and has not, to our knowledge, previously been reported in patients treated with high-frequency ventilation. The results of such treatment in 8 neonates seen in the Neonatal Intensive Care Unit, Wilford Hall USAF Medical Center, San Antonio, Texas, are presented. The mean gestational age was 35 weeks, and birth weight averaged 2.7 kg. The pneumopericardium developed while the patients were on high-frequency ventilation, and the diagnosis was confirmed with a chest radiogram. Treatment included pericardiocentesis with a needle catheter followed by placement of a 10F to 14F chest tube into the pericardial space. The pneumopericardium resolved in all 8 patients. Three of the newborns died of underlying disease; 5 survived and were discharged from the hospital. Pneumopericardium in the neonate is a life-threatening complication, and appropriate therapy includes drainage with a pericardial tube placed under direct vision.

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High-frequency ventilation (HFV) has been utilized with increasing frequency in neonatal intensive care units. Reports have demonstrated the benefits of HFV in patients with severe hyaline membrane disease [1, 2], pulmonary interstitial emphysema [3], and respiratory distress syndrome refractory to conventional ventilation [4, 5]. Studies have shown decreased barotrauma [6], gas exchange at lower airway pressure [7], and a reduction in the incidence of chronic lung disease with HFV compared with mechanical ventilation.

Numerous complications have been reported with HFV including necrotizing tracheobronchitis [8], pneumothorax [9], disruption of conduction airways [10], and hepatic fatty changes [11]. A recent review of the literature did not reveal any reports of neonatal pneumopericardium associated with the use of HFV. The present study reviews the experience at Wilford Hall USAF Medical Center with the management of this complication.

Material and Methods

The medical records of neonates treated at Wilford Hall USAF Medical Center from November 1982 to January 1988 were retrospectively reviewed. Two hundred seventy-three neonates were treated with HFV for respiratory failure. Pneumopericardium developed in 8 of them during treatment (Table 1).

The mean gestational age of these 8 patients was 35 weeks (range, 31 to 39 weeks); the mean birth weight was 2,684 g (range, 1,450 to 3,700 g); Apgar scores averaged 6 at one minute and 7 at five minutes. Five patients were born by cesarean section, 2 by spontaneous vaginal delivery, and 1 by low forceps delivery. Seven were male. The cause of the respiratory distress was hyaline membrane disease in 5 neonates, meconium aspiration in 2, and congenital viral pneumonia in 1. Only 2 of the infants were born at Wilford Hall USAF Medical Center; 6 were transferred from other institutions because of severe respiratory failure and pulmonary interstitial emphysema at one to ten days of age.

All 8 patients were eventually treated with HFV. One patient was placed on a Bird high-frequency respirator (VDR 1; Bird Space Technology, Sand Point, ID), characterized as a flow interrupter. The others were treated with high-frequency oscillatory ventilation (SS 1, Texas Research Inc, San Antonio, TX; or 3200, Gould Industries, Dayton, OH). Mean airway pressure and peak and trough oscillatory airway pressures were measured from the level of the endotracheal tube connector. A Hewlett-Packard 1280 B/C transducer and pressure module (model 78901A) were utilized to monitor and record proximal airway pressure.

Results

Tension pneumopericardium occurred within 24 hours of placement on high-frequency ventilators in 6 neonates, in 48 hours in 1, and in ten days in 1. Ventilator variables at the time of diagnosis included a mean inspired oxygen fraction of 0.82 (range, 0.55 to 1.00), a mean rate of 567 breaths per minute or 9.4 Hz (range, 360 to 1,260 breaths per minute or 6 to 21 Hz), peak oscillatory (inspiratory) pressure of 41 cm H_2O (range, 23 to 57 cm H_2O), trough airway pressure (constant positive airway pressure) of 8 cm H_2O (range, 4 to 12 cm H_2O), and a mean airway pressure of 25 cm H_2O (range, 14 to 33 cm H_2O).

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The opinions expressed are those of the authors and do not reflect the opinions of the United States Air Force or the Department of Defense.

Table 1. Summary of Patient Data

Patient No.	Sex	Date of Birth	Birth Weight (g)	Estimated Gestational Age (wk)	Diagnosis	FiO_2	CPAP (cm H_2O)	MAP (cm H_2O)	Respiratory Rate (breaths/min)	PIP (cm H_2O)	Apgar Score 1 Min	Apgar Score 5 Min	Outcome
1	M	11/6/82	2,870	38	Meconium aspiration	0.68	8	24	444	44	1	5	Died
2	F	3/24/83	1,600	32	Hyaline membrane disease	1.00	7	33	421	57	6	7	Died
3	M	5/22/83	1,658	31	Hyaline membrane disease	0.69	4	14	592	23	4	7	Survived
4	M	3/24/86	3,600	35	Hyaline membrane disease	0.55	7	19	1,260	32	9	9	Survived
5	M	4/24/86	3,540	36	Viral pneumonia	0.91	11	21	507	35	7	8	Survived
6	M	8/8/86	1,450	32	Hyaline membrane disease	1.00	9	31	472	51	9	9	Died
7	M	1/30/87	3,038	39	Meconium aspiration	1.00	6	28	360	48	6	7	Survived
8	M	1/5/88	3,700	37	Hyaline membrane disease	0.72	12	29	480	35	4	7	Survived
Average			2,684	35		0.82	8	25	567	41	6	7	

CPAP = continuous positive airway pressure; FiO_2 = inspired oxygen fraction; MAP = mean airway pressure; PIP = peak inspiratory pressure.

In all 8 infants, the pneumopericardium was seen clinically with hypotension and bradycardia. In addition, 5 infants manifested cyanosis. The diagnosis was confirmed by a chest radiogram in all 8 patients (Fig 1).

Pericardiocentesis was performed through a subxiphoid approach using sterile technique in the neonatal intensive care unit with a 20-gauge or 22-gauge angiocatheter. This initial emergency treatment was successful in all 8 neonates. However, the pneumopericardium recurred in all patients and necessitated placement of a 10F to 14F pericardial chest tube. One infant required two pericardial tubes to adequately decompress the tension pneumopericardium.

No patient died as a result of the tension pneumopericardium. However, 3 of the infants died of the underlying disease. Five infants ultimately recovered and were discharged.

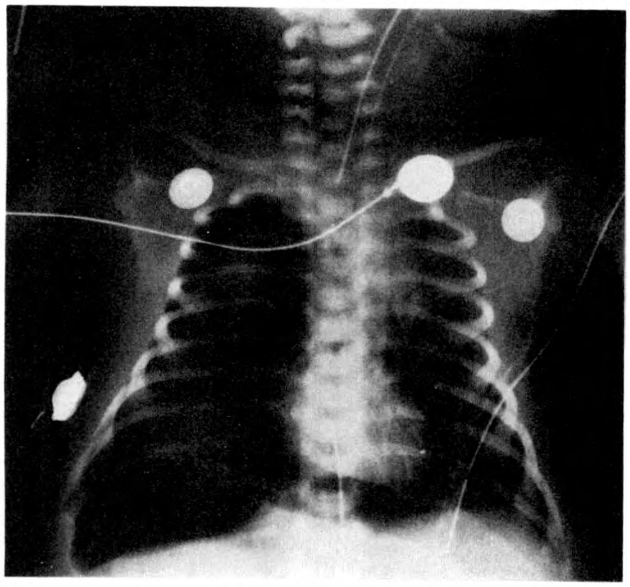

Fig 1. Radiogram demonstrating pneumopericardium and right pneumothorax in a neonate.

The technique of pericardial decompression utilized is similar to that described by Emery and colleagues [12]. The patients are prepared and draped using sterile technique in the neonatal intensive care unit. With local anesthesia, a subxiphoid vertical midline skin incision is made and continued through the linea alba. The pericardium is incised to permit anterior placement of a 10F to 14F chest tube. The tube is brought either through a separate stab incision or through the short upper vertical midline incision. The incision is then closed in two layers and the tube secured to the skin. The tube is connected to closed suction drainage. The tubes can be removed easily without complication after discontinuation of positive-pressure ventilation.

Comment

Before the development of intensive neonatal support, pneumopericardium in the neonate was uncommon. In 1970, only 7 cases of neonatal pneumopericardium were found in the literature [13]. With increasing usage of conventional ventilation, pneumopericardium has been reported with growing frequency. The published major series and our experience are summarized in Table 2 and comprise 156 patients. Overall, 73% of these patients survived the pneumopericardium, but only 32% were ultimately discharged from the hospital. This poor survival reflects the severe nature of the underlying disease process.

These newborn infants often require substantial positive-pressure ventilation. Alveoli or terminal airways rupture, thereby allowing air to dissect into the interstitial pulmonary tissue and produce pulmonary interstitial em-

Table 2. Reported Experience With Neonatal Pneumopericardium

Reference	Year	No. of Patients	Survival[a] Pneumopericardium	Survival[a] Overall
Higgins et al [14]	1979	12	5 (42)	4 (33)
Lawson et al [15]	1980	7	7 (100)	6 (86)
Burt and Lester [16]	1982	50	38 (76)	14 (28)
Cohen et al [17]	1983	13	11 (85)	6 (46)
Emery et al [18]	1984	47	35 (74)	12 (26)
Glenski and Hall [19]	1984	19	10 (53)	3 (16)
Neal et al [present report]	1989	8	8 (100)	5 (63)
Total		156	114 (73)	50 (32)

[a] Numbers in parentheses are percentages.

physema [20]. Further dissection of air along the pulmonary vessels results in pneumomediastinum [20, 21]. The air can also extend into the neck or peritoneum along vascular sheaths [20, 21], resulting in cervical subcutaneous emphysema or pneumoperitoneum, respectively. The anatomical pericardial communication with the mediastinum is probably along the great vessels [21, 22]. Postmortem examinations and anatomical studies have failed to reveal the exact site of entry [23].

Cohen and co-workers [17] evaluated the ventilatory variables in 13 neonates in whom pneumopericardium developed during positive-pressure ventilation. The mean peak inspiratory pressure was 42 mm Hg (range, 26 to 60 mm Hg). Glenski and Hall [19] found that pneumopericardium is associated with an elevated mean airway pressure greater than 17 cm H_2O and a peak inspiratory pressure of 32 ± 5 cm H_2O. These values for these variables are similar to those in this study.

Positive-pressure ventilation is often required to maintain adequate oxygenation in neonates with respiratory distress. High-frequency ventilation has been shown to maintain adequate gas exchange at lower airway pressures than conventional ventilators [3, 4, 7]. However, our study reveals that high mean airway pressures and high peak inspiratory pressures are sometimes necessary even with HFV. Manifestations of air-block syndrome, including tension pneumopericardium, can occur.

Neonates with tension pneumopericardium most frequently demonstrate hypotension, bradycardia, and cyanosis [16, 18]. These clinical findings associated with a mean airway pressure greater than 14 cm H_2O and a positive inspiratory pressure greater than 20 cm H_2O were indicative of a pneumothorax or pneumopericardium in this review. The diagnosis can be confirmed by chest radiogram [16–19] or transillumination of the thorax [24]. Treatment should include immediate pericardiocentesis with a 20-gauge or 22-gauge angiocatheter. Recurrence of pneumopericardium is common and occurred in all 8 of our patients. We therefore recommend placement of a subxiphoid pericardial tube as soon as possible. This procedure was associated with no morbidity in this study.

In conclusion, tension pneumopericardium can occur in neonates with high-frequency oscillatory ventilation at high mean airway pressures and high positive inspiratory pressures. These patients represent a surgical emergency. Immediate decompression by pericardiocentesis followed by placement of a pericardial tube is indicated.

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We thank the staff and fellows of the Neonatal Intensive Care Unit, Wilford Hall USAF Medical Center, for their assistance with this review.

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REVIEW OF RECENT BOOKS

The Esophagus: Medical and Surgical Management

Edited by Lucius Hill, Richard Kozarek, Richard McCallum, and C. Dale Mercer
Philadelphia, WB Saunders, 1988
327 pp, illustrated, $75.00

Reviewed by Robert J. Ginsberg, MD

This short (327-page) book deals with medical and surgical aspects of esophageal disease. The book is unique in bringing together surgeons and gastroenterologists in an attempt to present a comprehensive review of the subject. The editors and contributing authors on the most part reflect the extensive experience of the Virginia Mason Clinic, which has been a leader in the field of esophageal disease. Although all aspects of esophageal pathophysiology and treatment are dealt with, the book cannot be considered to be a reference textbook on the subject. In most instances, the management of specific entities reflects the attitudes of the Virginia Mason Group.

The senior author's interest in the surgical management of reflux disease is reflected in an excellent chapter describing in detail the Hill repair as well as the other currently utilized transthoracic and transabdominal repairs.

In many instances, the description of the surgical management of specific diseases fails to deal with the alternatives presently being utilized by surgeons (eg, resectional surgery for peptic strictures, standard techniques for Heller myotomy, alternative techniques for cricopharyngeal diverticulum operations).

Overall, the book is well-written, generously illustrated, and succinctly referenced. One wonders whether the extensive color illustrations and photographs in the front of the book add much to the overall volume. Artistic standardization of illustrations would be a welcome addition. As with other multiauthored books, there is variation in the readability and comprehensiveness of the various chapters, as well as occasional repetition.

As an overview of the medical and surgical management of esophageal disease as practiced by the Virginia Mason Clinic and its previous fellows, this book can be recommended. It is exceptionally readable and well-organized. This book can especially be recommended for those people training or trained in esophageal disease who wish to have a more in-depth knowledge of the practice of the highly eminent Virginia Mason Group.

Toronto, Ontario, Canada

Aortic Allografts: Reconstruction of Right Ventricle–Pulmonary Artery Continuity

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The use of aortic allografts in the repair of congenital cardiac lesions has increased as a result of both the advent of cryopreservation and the effects of increased donor availability secondary to infant transplantation. During the period 1986 through 1987, 38 cryopreserved aortic allografts were placed for right ventricle–pulmonary artery discontinuity. Size of the allografts ranged from 11 to 26 mm (mean size, 19 mm), and age of the patients ranged from 6 weeks to 26 years (mean age, 5 years). Twenty-one patients had primary placement of aortic allografts, and 17 underwent replacement of previous conduits. There were 5 hospital deaths (13%) overall, only 1 among the 10 patients younger than 6 months of age with truncus arteriosus, and none among the 17 patients having conduit replacement. A large conduit could be placed with a low incidence (10.5%) of postoperative hemorrhage related to the conduit. The aortic allograft is our conduit of choice for both conduit replacement and primary repair of right ventricle–pulmonary artery discontinuity.

(Ann Thorac Surg 1989;47:278–81)

The use of an aortic valve allograft in the repair of complex congenital cardiac malformations to reconstruct continuity between the right ventricle and the pulmonary artery was described by Ross and Somerville [1] in 1966. Complications in some of the early series led to discontinuation of use of these allografts by many groups and to initial interest in bioprosthetic valved conduits. When the limitations of such prostheses became evident, nonvalved conduits were advocated. In each case, serious limitations to their effectiveness have become evident, and thus, interest has again focused on the aortic valve allograft in the treatment of such patients. The advent of cryopreservation and increased donor availability secondary to infant transplantation have heightened this interest. This report describes our experience with cryopreserved aortic allografts for reconstruction of right ventricle–pulmonary artery continuity using a uniform operative technique for both primary repair and replacement of previous conduits.

Material and Methods

During the period of January 1986 through October 1987, 38 patients underwent repair of right ventricle–pulmonary artery discontinuity using a cryopreserved aortic allograft. Age ranged from 6 weeks to 26 years with a mean of 5 years (Fig 1). Conduit size ranged from 11 to 26 mm with a mean of 19 mm (Fig 2). Twenty-one patients had placement of the aortic allograft as a primary conduit repair (6 had had previous operative procedures), and 17 patients underwent replacement of previous conduits.

Aortic allografts in this series were procured by our transplantation team under sterile conditions at the time of transplant organ procurement. They were forwarded to CryoLife, Inc, under their protocol, frozen, and returned to our freezer unit. Thawing and preparation of the allografts again followed the CryoLife protocol with immediate use of the allografts.

The diagnoses and their prevalence are demonstrated in Figure 3, and the primary placement and replacement groups with types of lesions are presented in Table 1. The most common diagnosis was truncus arteriosus. Ten patients younger than 6 months of age underwent primary placement (no previous operative procedure) for this condition. There were 6 male and 4 female infants. Age ranged from 1.9 to 5.3 months (mean age, 2.9 months). The size of the conduits in this group ranged from 11 to 16 mm (mean size, 13.8 mm).

Replacement allografts were placed in 17 patients aged 4 to 26 years (mean age, 10 years) a mean of 96 months postoperatively. Conduit size ranged from 17 to 26 mm (mean size, 19.9 mm). Nine of these patients had had prior repair of truncus arteriosus, type I or II, a mean of 63 months postoperatively. The mean size of the replacement conduit for these patients was 19.4 mm.

A uniform operative technique was used. The aortic allograft was oriented with the mitral leaflet in the anterior position. The muscular rim of the previous septum was anastomosed within the ventricular cavity in the primary placement group and in the outflow tract in the replacement group. A Teflon felt pledgeted suture was passed through muscle and used to anchor the muscular ridge within the ventricular outflow tract. In the case of the primary placement group it was tied to the ventricular septal defect patch, whereas in the case of the replacement group it was placed within the outflow tract itself. The suture line was then begun within the cavity and brought out to the free wall. Here the previous mitral valve was used as a patch, with augmentation with

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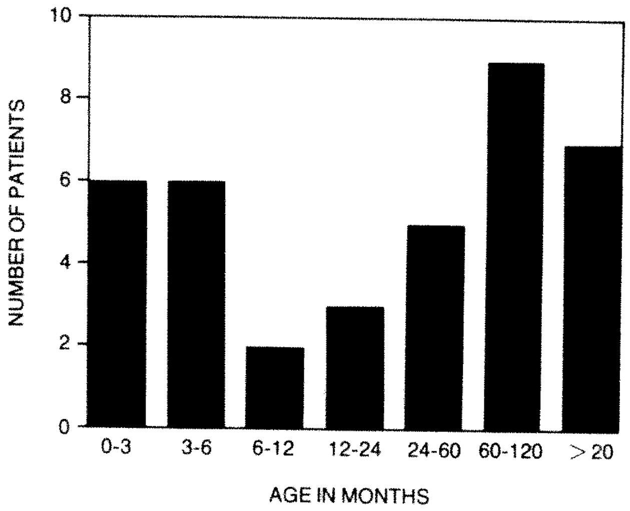

Fig 1. Patient population by age.

pericardium as necessary to complete the outflow tract closure.

The 30-day in-hospital mortality and postoperative complications were reviewed, and echocardiographic evaluation was done for evidence of conduit stenosis or insufficiency in 31 of the 38 patients. Results were noted for the entire cohort and for two subsets: those having primary repair of truncus arteriosus who were younger than 6 months of age and the group having conduit replacement.

Results

The 30-day in-hospital mortality among the 38 patients in this series was 13% (5 patients). There was only 1 possible conduit-related death. One death occurred in the infant truncus group secondary to an acute pulmonary hypertensive crisis on the second postoperative day (1/10 or 10%). The remaining 4 deaths were in the complex placement group (patients having primary repair or primary conduit repair excluding the 10 infants with truncus arteriosus): 3 of the patients had undergone primary placement and 1 had had prior operative procedures (4/11 or 36%). There were no deaths in the replacement group.

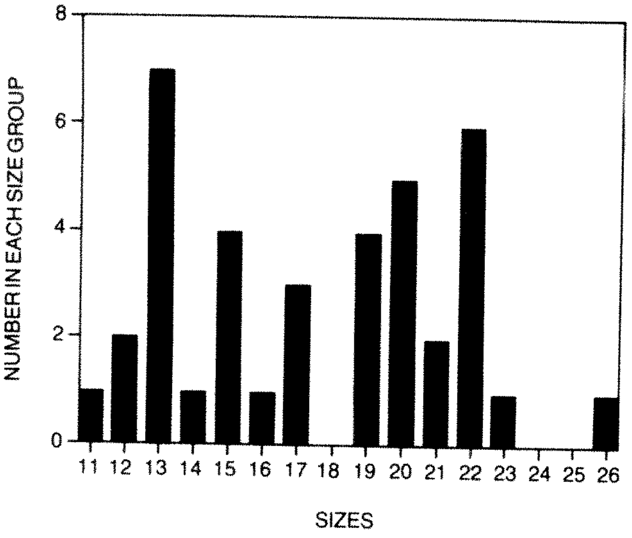

Fig 2. Allograft sizes from 11 to 26 mm. Note the two populations: the primary placement group with an allograft less than 17 mm in diameter and the replacement group with an allograft greater than 17 mm in size.

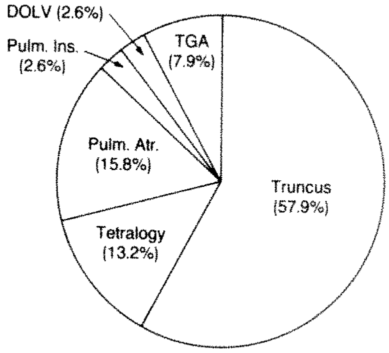

Fig 3. Diagnoses and incidence in this series. (DOLU = double-outlet left ventricle; Pulm. Atr. *= pulmonary atresia;* Pulm. Ins. *= pulmonary insufficiency;* TGA *= transposition of the great arteries.)*

The ages of the 4 patients who died with complex lesions ranged from 8 to 14 months. The diagnoses included the following: truncus arteriosus type II with truncal valve insufficiency in a 10-month-old infant; transposition of the great arteries, ventricular septal defect, pulmonary stenosis, and subaortic stenosis in a 13-month-old infant; truncus arteriosus type I with pulmonary hypertension in an 8-month-old infant; and pulmonary atresia and ventricular septal defect in a 12-month-old infant who had undergone multiple prior procedures. Only in the 13-month-old infant was there a possible relationship between placement of the allograft and death. In this patient, sudden low cardiac output, renal failure, and pulmonary edema developed eight hours postoperatively. This raised concern that either a transfusion reaction (which was not documented) or a reaction to the allograft nutrient media, calf serum, (which likewise could not be documented) had occurred.

Table 1. Types of Lesions in the Two Groups

Lesion	Primary	Replacement	Total
Truncus arteriosus (<6)	10	9	19
Truncus arteriosus (>6 PA band)	3	0	3
Pulmonary atresia + IVS	1	0	1
Pulmonary atresia + VSD	3	3	6
Transposition of great arteries	2	1	3
Tetralogy of Fallot	2	3	5
Double-outlet left ventricle	0	1	1
Total	21	17	38

IVS = intact ventricular septum; PA = pulmonary artery; VSD = ventricular septal defect.

Postoperative hemorrhage occurred in 7 patients. Two episodes were in the infant truncus group, and only one episode involved the conduit itself. Two were in the replacement group, and again one episode involved the conduit anastomosis. Three were in the complex placement group, with two from the conduit anastomoses. Hence, 4 of the 38 patients had hemorrhage that was conduit related, an incidence of 10.5%. There was 1 case of fungous endocarditis 3 weeks postoperatively, which was treated with amphotericin B. No deep or mediastinal infections occurred.

Complete heart block occurred in 2 patients. In 1 it was transient, resolving on the seventh postoperative day. The other patient required permanent pacemaker placement.

Echocardiographic evaluation was performed early in 31 of the 38 patients. Mild valvular insufficiency was noted in 13, 5 in the infant truncus group and 5 in the conduit replacement group. Major stenosis was identified in 5 patients in the conduit replacement group, with gradients ranging from 10 to 40 mm Hg. However, none of the stenoses were valvular. Also, the stenoses occurred in patients without truncus arteriosus (5/8), and were related to distal angulation of the allograft reconstruction.

Comment

The use of the aortic allograft in the repair of congenital cardiac lesions has undergone a resurgence because of reports of excellent long-term results, the advent of cryopreservation, and increased donor availability secondary to infant transplantation. However, the major impetus for exploring the aortic allograft has been the failure of both Dacron porcine-valved heterograft conduits and the nonvalved conduits in long-term follow-up, and the disappointing results with these techniques.

The current series explores an early experience with the aortic allograft as a conduit for repair of right ventricle–pulmonary artery discontinuity. In this series, 21 primary placements and 17 replacements of previous conduits were performed. Of importance is the large number of allografts placed in infants, including patients with truncus arteriosus who were younger than 6 months of age. Thus, this series represents two distinct experiences—the infant primary placement group and the replacement conduit group (see Figs 2, 3).

With reference to the infant primary placement group, 17 of the 21 primary placements in the series were performed in patients younger than 24 months of age. Since 1966 when Ross and Somerville [1] reported an aortic allograft repair, many authors have described the use of this method for right ventricle–pulmonary artery discontinuity. However, only a relatively small number of infants have undergone primary placement. Fontan and associates [2] in 1984 described their experience with aortic allografts in 93 patients. The youngest was 7 months old, and the small number in the infant group had an increased mortality. In commenting on that report, Barratt-Boyes described an experience with 13 patients followed for 4 to 9 years. Excellent late results were noted, with no complications of rupture or infection. Further, he pointed out that in most instances a larger-diameter allograft could be placed than would otherwise be possible.

In the current series, the mortality among patients having primary repair of truncus arteriosus type I who were younger than 6 months of age was 10%. In this subgroup, only 2 patients experienced postoperative hemorrhage, and in only 1 of them was the site of hemorrhage the conduit anastomosis. This differs substantially from our previous experience [3] with 12-mm Dacron porcine-valved conduits, in which a 40% incidence of hemorrhage was noted. A larger-sized conduit (mean size, 13.8 mm) was placed in the infants in the present series, a group of patients in whom a 12-mm Dacron conduit would most commonly be placed. Further, pseudointimal proliferation, common as a cause of infant conduit replacement [3, 4], is eliminated by the use of an aortic allograft.

Finally, the use of the allograft as a valved conduit in the infant group provides a functional pulmonary valve in the early postoperative period. Although Spicer and colleagues [5] reported the use of valveless conduits in such infants, the presence of a valve in the pulmonary arterial bed should decrease the risk of pulmonary hypertensive episodes. Boyce and co-workers [3] noted a 46-month mean conduit survival in the 12-mm Dacron porcine-valved right ventricle–pulmonary artery extracardiac conduit. The obstructions occurred at multiple levels, although pseudointima and valve destruction were common [3, 6, 7]. With use of the larger sizes and avoidance of such stenoses, substantial improvement in longevity can be expected.

Among the remaining 11 patients in the primary placement group, there were 4 deaths, all in the group younger than 24 months of age. Only in the patient with transposition of the great arteries, ventricular septal defect, pulmonary stenosis, and subaortic stenosis could an allograft-related complication be associated with the death. This case is of importance, however, because there is concern about the immunological stimulus such allografts can present and the potential for a hyperimmune response to either the allograft or its nutrient media (in this case, calf serum).

The replacement group in this series comprised 17 patients, 9 of whom had had previous conduit placement for truncus arteriosus. In this group, replacement would previously have been accomplished by using either a Dacron porcine-valved extracardiac conduit or a nonvalved Gore-Tex patch or tube graft. The former method is subject to the same degenerative changes in the porcine valve as in small conduits, with the potential for pseudointimal proliferation, as well as conduit stenosis at proximal and distal anastomoses. The latter method of repair, although the subject of much enthusiasm in recent years, appears subject to the same pseudointimal problems as well as compression from adjacent structures, thus producing kinking of the ridged conduit material.

In this series with the aortic allograft, there were no operative deaths, which is comparable to the low mortality at reoperation noted in previous series [3, 7]. A mean allograft size of 19.9 mm was possible in the replacement group, and only two episodes of postoperative hemorrhage were encountered. No infectious complications were seen in the replacement group, and no gross immunological reactions occurred. In 5 of the 8 patients undergoing replacement for a cause other than truncus arteriosus, echocardiographic evidence of early stenosis of the conduit distal to the valve reflected the tortuous course through previous scar tissue of these replacement conduits. In the complex subgroup, close observation will be necessary to determine if further compression from scar ingrowth will occur.

Aortic allografts for reconstruction of right ventricle–pulmonary artery continuity can be used with an acceptable mortality and low morbidity. The conduit itself provides an excellent material for reconstruction with a low incidence of postoperative hemorrhage and infectious complications. Early results are encouraging; with the use of this type of repair, a larger-sized conduit can be placed, fewer conduit replacements may be necessary, and problems of conduit degeneration may be reduced. The aortic allograft is currently our conduit of choice for both primary repair and conduit replacement in patients with complex congenital cardiac defects requiring right ventricle–pulmonary artery reconstruction.

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Diagnosis of Traumatic Thoracic Aortic Rupture: A 10-Year Retrospective Analysis

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A 10-year retrospective analysis of 82 patients with suspected thoracic aortic rupture (TAR) due to blunt chest trauma was performed to define which symptoms and signs were helpful in making an early diagnosis. Symptoms and signs associated with TAR included midscapular back pain (in the absence of thoracic spine fracture), unexplained hypotension, upper extremity hypertension, bilateral femoral pulse deficits, and initial chest tube output in excess of 750 mL. Chest roentgenographic signs seen with significantly greater frequency in the 12 patients with TAR than in 70 patients without such rupture included a widened paratracheal stripe (7 patients), deviation of the nasogastric tube or central venous pressure line (5 patients), blurring of the aortic knob (9 patients), abnormal paraspinous stripe (6 patients), and rightward tracheal deviation (5 patients). Mediastinal widening of greater than 8 cm occurred in 11 of the 12 patients with TAR (sensitivity, 92%); its specificity, however, was only 10% (11 true-positive and 63 false-positive results). In patients in hemodynamically stable condition who display these findings, immediate aortography should be considered. The presence of myocardial contusions, intraabdominal injuries, and pelvic fractures also occurred more frequently in patients with TAR. We conclude that a detailed history, physical examination, and chest roentgenography, with rapid progression to aortography in suspicious cases, represent the safest and most reliable approach to patients with TAR.

(Ann Thorac Surg 1989;47:282–6)

Thoracic aortic rupture (TAR) secondary to blunt chest trauma is a devastating injury that can be expected to kill more than 90% of its victims if definitive surgical correction is not promptly performed [1]. Aortography is well established as the "gold standard" for establishing the diagnosis of TAR; however, it is often delayed or not performed because of overlooked subtle physical and radiographic signs. Although mediastinal widening seen on chest roentgenograms has been described as the most consistent sign of TAR [2–8], a host of additional chest roentgenographic and clinical findings have been suggested as indications for aortography [3–23].

The purpose of the present retrospective study was to determine which clinical and chest roentgenographic signs were most valuable in distinguishing blunt chest trauma victims with TAR from those without such rupture to define indications for selecting patients for aortography. During the past 10 years, 82 patients suspected of having TAR were evaluated by history, physical examination, chest roentgenography, and aortography; these patients form the basis of this study.

Material and Methods

During the 10-year period of January 1978 to January 1988, 82 patients suspected of having TAR were evaluated. The cause of injury was a motor vehicle accident in 54 patients, motorcycle accident in 13, motor vehicle versus pedestrian accident in 6, and fall from a height in 9. Patients suspected of having vascular injuries other than TAR were excluded from the study. The patients ranged in age from 14 to 76 years (mean age ± standard deviation, 36 ± 16 years). Sixty-eight patients were male and 14 were female.

The medical records of all patients with suspected TAR were retrospectively analyzed for the presence or absence of relevant clinical findings (Table 1). The admission anteroposterior chest roentgenograms, which were usually obtained using a portable machine and a 100-cm source–image distance, were retrospectively analyzed for relevant findings; 12 chest roentgenograms could not be retrieved for review. All of the latter were from patients subsequently found not to have TAR. Specific roentgenographic findings sought are shown in Table 2.

Results

Of the 12 patients with TAR, 9 were involved in motor vehicle accidents and 3 were victims of motorcycle accidents; none of the patients involved in a motor vehicle versus pedestrian accident and none of the patients who sustained a fall had TAR. Complaints of midscapular back pain were found in 12 (20%) of 61 alert patients; 3 of these patients were subsequently found to have TAR, whereas 8 others had thoracic spine fractures as the cause of the back pain. Thus, 3 (75%) of 4 patients with midscapular back pain and no thoracic spine fracture had TAR.

The presence of upper extremity hypertension or bilat-

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Table 1. Incidence and Positive Diagnostic Yield of Symptoms and Signs in 82 Patients With Suspected Traumatic Thoracic Aortic Rupture

Symptom or Sign	Patients With Thoracic Aortic Rupture (n = 12)	Total (n = 82)	Positive Diagnostic Yield (%)
Chest pain	7	39	18
Midscapular back pain	3	12	25
Dyspnea	2	10	20
Hoarseness	0	1	0
Cough	0	1	0
Hemoptysis	0	1	0
Coma	5	21	24
Hypotension[a]	7	14	50
External chest injury	4	24	17
Bilateral femoral pulse deficit[a]	2	2	100
Systolic ejection murmur	2	7	29
Upper extremity hypertension[a]	3	3	100
Subcutaneous emphysema	2	12	17
Hematocrit less than 30%	2	10	20
Hemothorax greater than 750 mL[a]	2	2	100

[a] This occurred more frequently in patients with thoracic aortic rupture than in those without it ($p < 0.05$).

eral decreased femoral pulses occurred with greater frequency in patients with TAR than in those without it ($p < 0.001$); most patients with TAR, however, did not have these findings. A history of substantial hypotension also occurred with greater frequency in patients found to have TAR ($p < 0.05$); 6 of the 12 patients with TAR had hypotension. Of the 12 patients with TAR, 7 (58%) had no external evidence of chest trauma. Only 2 patients in the series had initial chest tube outputs greater than 750 mL; both of them were subsequently found to have TAR. There was also a significantly greater incidence of myocardial contusions, intraabdominal injuries, and pelvic fractures in patients with TAR than in those without it ($p < 0.05$).

A widened mediastinum seen on the initial chest roentgenogram was the major indication for aortography in 74 patients (90%); of these, 11 patients (15%) had TAR. Indications for aortography included mediastinal widening in 74 patients, isolated upper rib fractures in 5, isolated apical cap in 1, pneumomediastinum in 1, and isolated nasogastric tube deviation in 1. One of the patients without mediastinal widening was found to have TAR. The indication for aortography in this patient was nasogastric tube deviation.

Eleven of the 12 patients with TAR had a widened mediastinum on the chest roentgenogram, resulting in a 92% sensitivity for diagnosing TAR using this roentgenographic finding; the specificity, however, was only 10%. The positive predictive value of a widened mediastinum in diagnosing TAR was 15%.

Chest roentgenographic findings seen with significantly greater frequency in patients with TAR compared with those without such rupture ($p < 0.05$) included blurring of the aortic knob, a widened right paratracheal stripe, a distorted paraspinous stripe, opacification of the aortopulmonary space, and deviation of the nasogastric tube or central venous pressure line to the right (Figs 1, 2). Deviation of the trachea was seen in 5 (42%) of the 12 patients with TAR; 7 (87.5%) of 8 other patients with rightward tracheal deviation but without TAR were elderly and had tortuous aortas. A hemothorax was noted in 6 (50%) of the 12 patients with TAR and in 19 (33%) of 58 patients without rupture.

Angiographic complications occurred in 8 patients (10%) and consisted mostly of groin hematomas that resolved without sequelae. Seven patients in the series died; 3 patients with TAR died perioperatively secondary to cardiac injury and 4 patients without rupture died of other injuries.

Comment

Data from the present study indicate that more than half of patients with TAR can be expected to have no visible external signs of chest trauma. Furthermore, it may be impossible to elicit symptoms in a substantial number of patients because of altered mental status due to head trauma. A high index of suspicion should be maintained

Table 2. Incidence and Positive Diagnostic Yield of Chest Roentgenographic Signs in 74 Patients With Suspected Traumatic Thoracic Aortic Rupture

Sign	Patients With Thoracic Aortic Rupture (n = 12)	Total (n = 82)	Positive Diagnostic Yield (%)
Widened mediastinum	11	74	15
Widened paratracheal stripe[a]	7	11	64
Deviated nasogastric tube[a]	4	4	100
Deviated central venous pressure line[a]	2	2	100
Blurred aortic knob[a]	9	32	28
Abnormal paraspinous stripe[a]	6	20	30
Deviated trachea	5	13	38
Opacified aortopulmonary space	6	23	26
Apical cap	3	19	16
Depressed left mainstem bronchus	1	1	100
Hemothorax	6	25	24
First rib fracture	3	13	23
Second rib fracture	3	15	20

[a] This occurred more frequently in patients with thoracic aortic rupture than in those without it ($p < 0.05$).

in all patients sustaining high-speed deceleration chest trauma, especially those having unexplained hypotension or midscapular back pain not caused by thoracic vertebral fracture. All too often, medical attention is diverted to other coexisting injuries such as intraabdominal injuries, pelvic fractures, and myocardial contusions; as shown in the present series, these occur with increased frequency in blunt chest trauma patients who also have TAR [24].

As confirmed by this and other published reports, mediastinal widening seen on standard chest roentgenograms is the most sensitive diagnostic sign of TAR; it occurred in 92% of the patients with TAR in the present series. Its specificity, however, was only 10.0%. A mediastinal width of greater than 8 cm on standard anteroposterior chest roentgenograms mandates aortography in the patient in hemodynamically stable condition. In the present series, the mediastinal width at the level of the aortic knob in patients with TAR ranged from 7.5 to 12.0 cm. Although uncommon, TAR can be present in patients having a mediastinal width within normal limits (Fig 3).

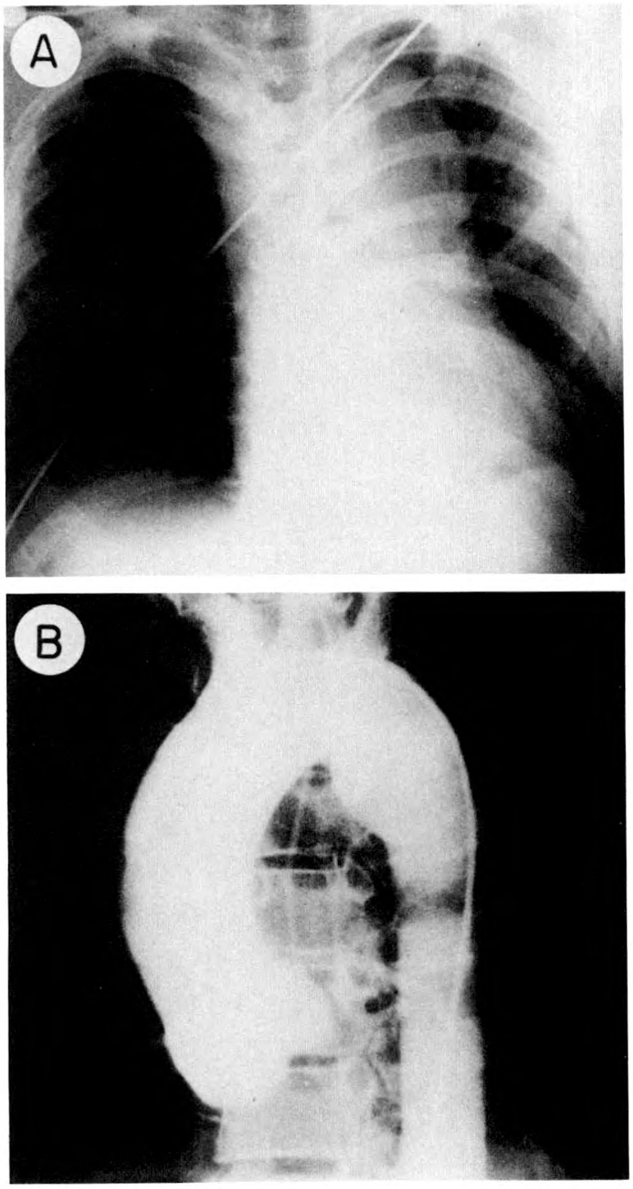

Fig 1. (A) Chest roentgenogram of a patient who was in an automobile accident and sustained thoracic aortic rupture. Note the mediastinal widening and abnormal paraspinous stripe. (B) Aortogram of the same patient reveals the rupture.

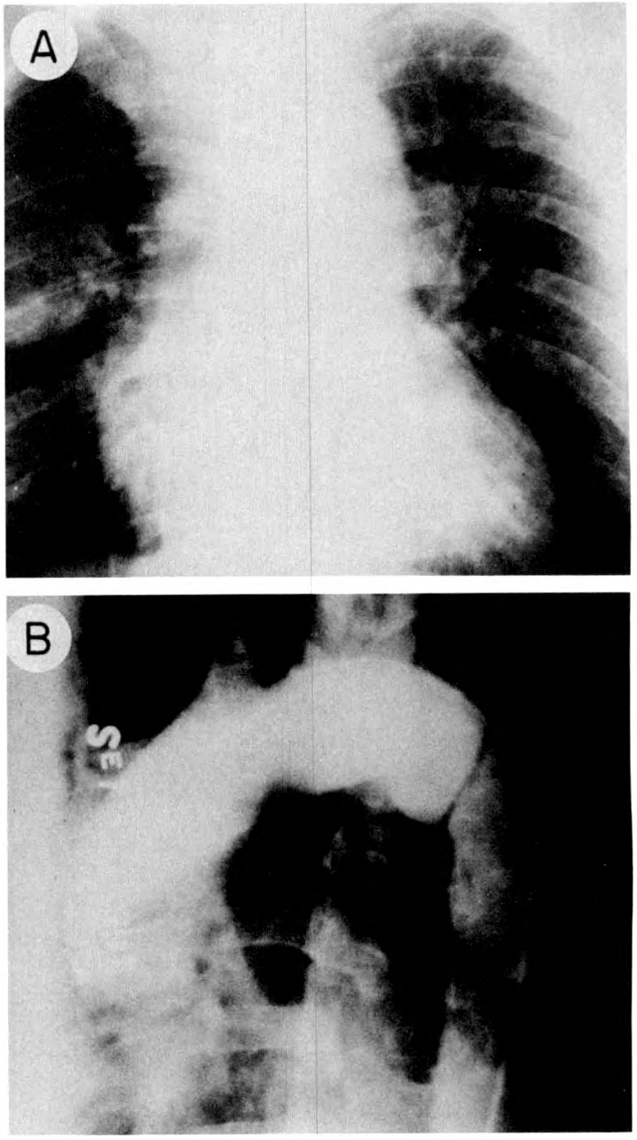

Fig 2. (A) Chest roentgenogram of a patient who was in a motorcycle accident and sustained thoracic aortic rupture. Note the widened mediastinum, deviated nasogastric tube, blurred aortic knob, and opacification of the aortopulmonary space. (B) Aortogram of the same patient reveals the rupture just distal to the left subclavian artery.

Additional chest roentgenographic findings seen more often in blunt chest trauma patients with TAR than in those without rupture included a widened right paratracheal stripe, opacification of the aortopulmonary space, rightward deviation of the nasogastric tube or central venous pressure line, blurring of the aortic knob, and an abnormal paraspinous stripe. Of the 5 patients with upper rib fractures as the sole indication for aortography, none

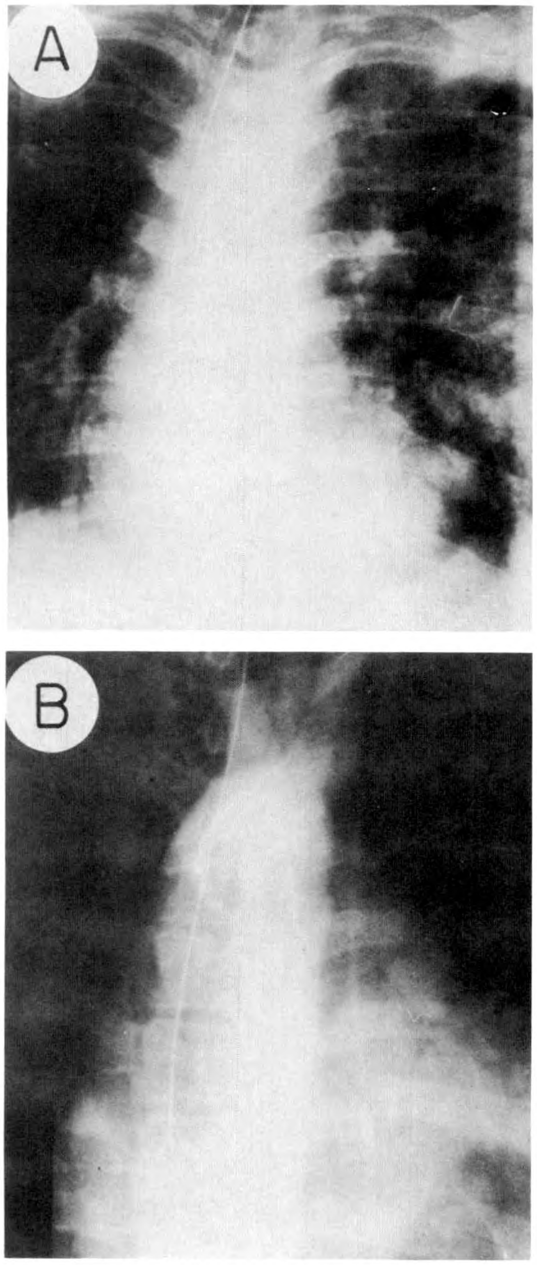

Fig 3. (A) Chest roentgenogram of a patient who was in a motor vehicle accident and sustained thoracic aortic rupture. Note the normal mediastinal width (7.5 cm) and deviated nasogastric tube. (B) Aortogram of the same patient reveals the rupture distal to the left subclavian artery.

were subsequently found to have TAR. Thus, upper rib fracture unassociated with other positive findings does not appear to be an important indication for aortography in patients sustaining blunt chest trauma.

Although computed tomography has been suggested as an accurate method for diagnosing TAR secondary to blunt chest trauma [25], aortography remains the gold standard for making the diagnosis. One patient in the present series with multiple chest roentgenographic findings consistent with TAR underwent chest computed tomography only to have the diagnosis of TAR missed, resulting in a delay in diagnosis and surgical correction. Although retrospective analysis of the computed tomographic scan revealed mediastinal fluid, aortic deformity was absent. We currently recommend the use of aortography, rather than chest computed tomography, as the best method of diagnosing TAR in patients sustaining high-speed deceleration chest trauma. A prospective study comparing chest computed tomography and aortography in the diagnosis of TAR is lacking but would be expected to yield further information regarding the limitations of chest computed tomography in the diagnosis of TAR. Intraarterial digital subtraction angiography, on the other hand, may be faster, less expensive, and as accurate as standard aortography in making the diagnosis of TAR [26], but confirmatory studies are necessary before this method can be accepted as the best method for diagnosing TAR.

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Effect of Cold Cardioplegic Solution and Hypothermia on Response to Acetylcholine in Perfused Epicardial Coronary Artery of Pig

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The effect of cold cardioplegic solution and hypothermia on the response to acetylcholine, a major postganglionic neurotransmitter of the parasympathetic nervous system, was studied using perfused epicardial coronary arteries of pigs. Cold crystalloid cardioplegic solution (5°C) and hypothermia including topical cooling with slushed ice significantly augmented the coronary flow reduction by acetylcholine at one and two hours after rewarming. Cold Krebs-Henseleit solution (5°C) with hypothermia showed similar effects. However, cardioplegic solution at 37°C did not affect the responsiveness. The coronary flow reduction induced by potassium chloride (60 mmol/L) did not change even after the administration of cold cardioplegic solution (5°C) or cold Krebs-Henseleit solution (5°C), indicating that cooling did not necessarily augment the coronary contractile response generally. It is concluded that cooling and subsequent rewarming can potentiate the contractile response of the coronary artery of the pig to acetylcholine. This suggests that cold cardioplegic solution with hypothermia can promote intraoperative coronary spasm upon activation of the parasympathetic nervous system.

(Ann Thorac Surg 1989;47:287–92)

Even though improvements in cardioplegia and hypothermia have achieved a lowered incidence of perioperative myocardial infarction and a decreased operative mortality in patients undergoing coronary artery bypass grafting procedures [1], at present, perioperative myocardial infarction remains one of the serious complications of open heart operations, and its pathogenesis is a matter of conjecture. Several investigators [2–7] have reported that spasm of the epicardial coronary artery was observed in some instances of perioperative myocardial ischemia, and most of the perioperative coronary spasms were noticed within a few hours after cardioplegia was finished. Furthermore, it has been suggested that the abnormal discharge of the parasympathetic nervous system plays an important role in the pathogenesis of coronary spasm [8, 9], and that the perivascular nerve stimulation of the epicardial coronary artery causes vasoconstriction through the activation of the cholinergic mechanism in pigs [10].

Although many experimental and clinical observations have shown the benefit of cardioplegia and hypothermia in the preservation of myocardial integrity [11, 12], we are aware of no studies examining the effect of cardioplegia and hypothermia on the reactivity of the coronary artery. The purpose of this study is to investigate the effect of a cold cardioplegic solution with hypothermia on the responsiveness of the coronary artery to a parasympathetic neurotransmitter, acetylcholine.

Material and Methods

Experimental Preparation and Perfusion Technique

Pig hearts were obtained from a slaughterhouse and were immediately placed in Krebs-Henseleit solution. The left ventricle perfused by the left anterior descending coronary artery was excised. Figure 1 illustrates the experimental preparation. Both ends of the epicardial left anterior descending coronary artery for about 4.0 cm were cannulated with polyethylene cannulas. After the ligation of all side branches, coronary arteries with excised left ventricles were mounted on a warm organ bath and perfused at a constant pressure of 80 mm Hg with Krebs-Henseleit solution. The solution was oxygenated with a gas mixture of 95% oxygen and 5% carbon dioxide at a temperature of 37°C and a pH of 7.35 to 7.45, and was recirculated. The composition of the Krebs-Henseleit solution in millimoles per liter was as follows: Na^+, 141.0; K^+, 5.9; Ca^{2+}, 2.6; Mg^{2+}, 1.0; SO_4^{2-}, 1.0; $H_2PO_4^-$, 1.0; HCO_3^+, 20.0; Cl^-, 131.1; and glucose, 10.0.

Proper resistance was placed at the distal site of the outflow cannula to prevent collapse of the vessel. The external surface of the coronary artery was not bathed with the solution but was exposed to warm, humid air in the organ bath. Coronary flow was measured by an electromagnetic flowmeter (model MF26, Nihon-kohden, Tokyo, Japan), and perfusion pressure was measured by an electronic manometer (Nihon-kohden model MPU-0.5A) placed at the site of the inflow cannula. Outputs from the flowmeter and electronic manometer were recorded on a pen writing recorder (Nihon-kohden model PMP 3004). The drug used was acetylcholine chloride (Daiichi Pharmaceutical Co, Tokyo, Japan). Potassium

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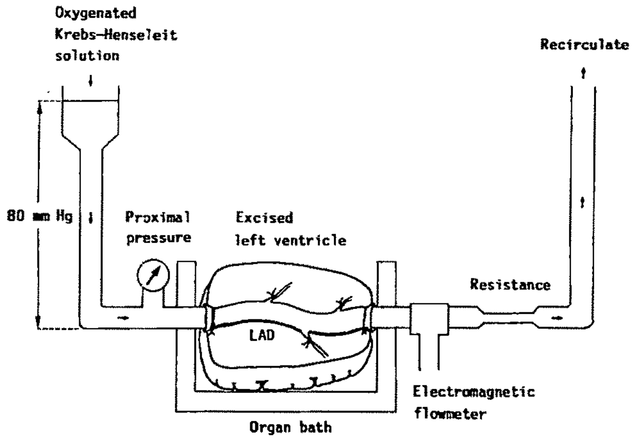

Fig 1. Experimental preparation. (LAD = left anterior descending coronary artery.)

chloride was used to induce coronary contraction not related to receptor activation, that is, to cause contraction of vascular smooth muscle by direct depolarization of the cell membrane and subsequent calcium influx.

Hypothermia and Administration of Cardioplegia

The temperature of the circulating Krebs-Henseleit solution was reduced from 37°C to 30°C in 30 minutes before cardioplegia was administered. The excised pig heart was covered with slushed ice (frozen Krebs-Henseleit solution) during cardioplegia. After 60 minutes of cardioplegia, the preparation was reperfused with Krebs-Henseleit solution at a temperature of 30°C, and was returned to 37°C in 30 minutes. The temperature of the coronary artery was monitored by a microthermometer inserted between the coronary artery and the adjacent ventricular muscles. At the beginning of the administration of cardioplegia, the temperature of the preparation was about 32°C; it was decreased to about 8°C within five minutes and was kept almost stationary during cardioplegia. Then the temperature of the preparation was elevated to 37°C within 35 minutes by rewarming the circulating Krebs-Henseleit solution.

Crystalloid cardioplegic solution was prepared each morning and was similar to that used in clinical practice. The solution consisted of 5% dextrose in distilled water including potassium chloride (20 mmol/L), sodium bicarbonate (8 mmol/L), and regular insulin (20 U/L). The cardioplegic solution was given intermittently every 15 minutes during the 60 minutes of cardioplegia with an infusion pressure of 100 mm Hg immediately after circulation of the Krebs-Henseleit solution had been stopped. The initial volume of the cardioplegic solution was 500 mL and the subsequent volume was 300 mL.

Experimental Protocol

The experimental protocol is depicted in Figure 2. All experiments were preceded by a two-hour control period during which the stability of the preparation was confirmed. The effects of acetylcholine (10^{-5} to 10^{-8} mol/L) on coronary flow were examined before (control) and one, two, and three hours after the administration of the cardioplegic solution or Krebs-Henseleit solution. Changes in coronary flow induced by potassium chloride (60 mmol/L) were also examined before and 1.5 hours after infusion of the solution.

Experimental Groups

Experiments were carried out in four groups of 8 hearts each (see Fig 2). Group 1 received cardioplegic solution at 5°C with hypothermia; group 2, cardioplegic solution at 37°C without hypothermia; group 3, Krebs-Henseleit solution at 5°C with hypothermia; and group 4, Krebs-Henseleit solution at 37°C without hypothermia.

Statistical Analysis

All values are expressed as the mean ± the standard error of the mean. Statistical analysis was done using Student's paired *t* test for two-paired data. The significance of the difference in ED_{50} (defined as the concentration of the agonist at which 50% of the maximum response was obtained) was tested by unpaired *t* test. The data obtained from repeat measurement studies were compared using analysis of variance and the modified *t* test (Tukey's method), and data between the two groups were compared at each measuring point using the unpaired *t* test. Significance was defined by a *p* value of less than 0.05.

Results

Responses to Acetylcholine

The flow rate through the isolated epicardial coronary artery became stable within 30 minutes after the start of

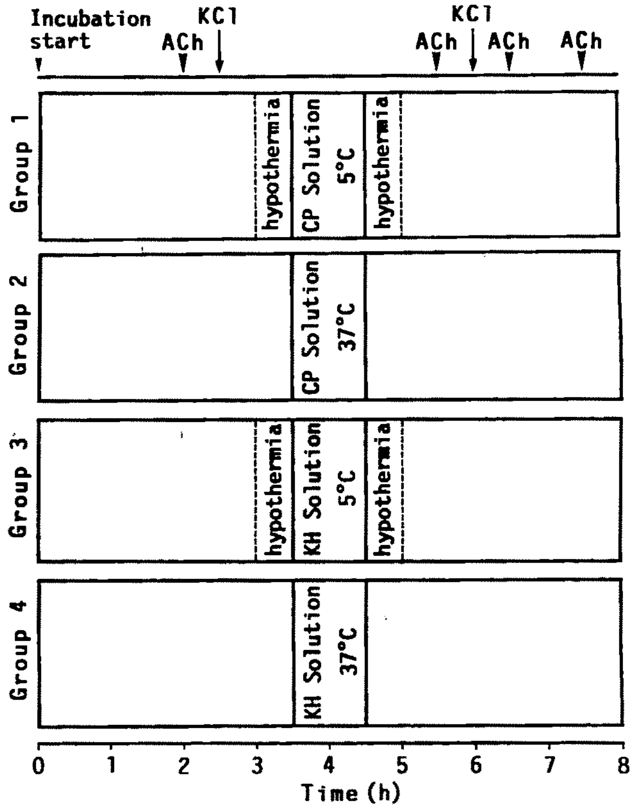

Fig 2. Experimental protocol in the four groups. Each group consisted of 8 pig hearts. (ACh = acetylcholine; CP = cardioplegic; KCl = potassium chloride; KH = Krebs-Henseleit.)

perfusion with normal Krebs-Henseleit solution, and the basal flow rate did not change throughout the experimental period in all groups (77.8 ± 2.8 mL/min in group 1; 90.5 ± 2.2 mL/min in group 2; 82.9 ± 3.3 mL/min in group 3; and 82.9 ± 2.3 mL/min in group 4).

Figure 3 shows representative tracings of coronary flow reduction induced by acetylcholine before and after the administration of cold cardioplegia with hypothermia (group 1). Coronary flow decreased in a dose-dependent manner. The degree of flow reduction was augmented at one hour after cardioplegia, from 52 mL/min to 77 mL/min at 10^{-5} mol/L, but the threshold dose (10^{-7} mol/L) did not change. In one instance in this group, acetylcholine (10^{-5} mol/L) caused a marked percent flow reduction to 18% of the control value at one hour after cardioplegia.

The upper panel of Figure 4 summarizes the percent coronary flow reduction induced by acetylcholine (10^{-5} mol/L) before and after the administration of cardioplegia (group 1). The percent flow reduction was significantly augmented at one and two hours after cardioplegia (25.5% ± 6.2% during the control period versus 45.0% ± 12.3% and 40.5% ± 12.3% at one and two hours after cardioplegia administration, respectively). Three hours after infusion of the cardioplegic solution, however, the response to acetylcholine was comparable with that seen during the control period (23.0% ± 9.6% at three hours).

The lower panel of Figure 4 summarizes the percent coronary flow reduction induced by acetylcholine (10^{-5} mol/L) in group 2 (cardioplegic solution at 37°C with normothermia). The magnitude of the responses did not change significantly (19.1% ± 6.1% during the control period, and 20.4% ± 6.6%, 20.6% ± 5.6%, and 19.6% ± 5.3% at one, two, and three hours after infusion of the cardioplegic solution, respectively).

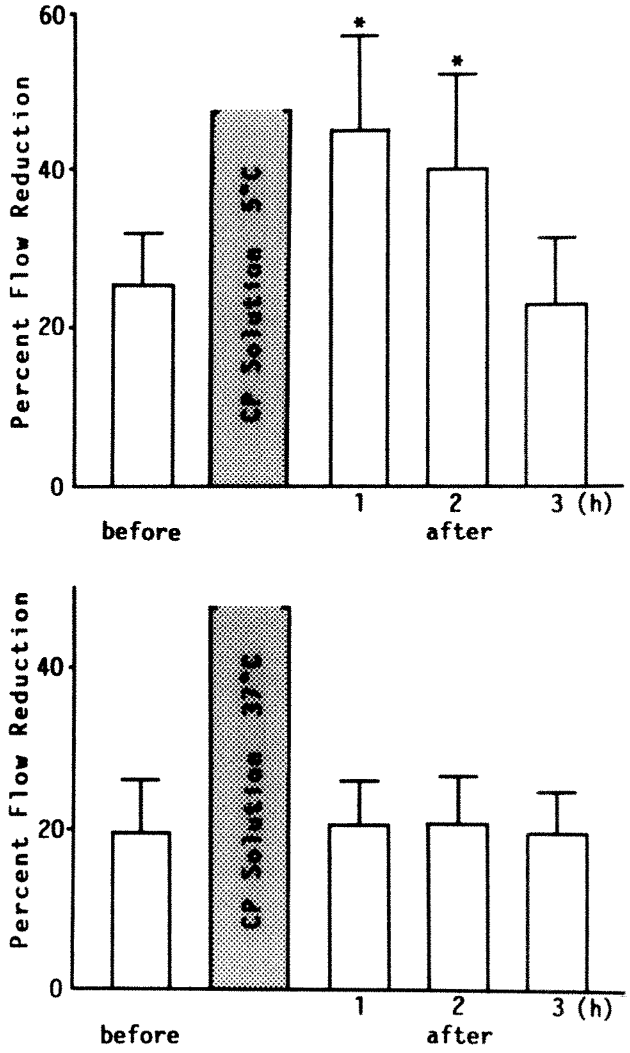

Fig 4. Percent flow reduction induced by acetylcholine chloride (10^{-5} mol/L) before and after the administration of cardioplegic (CP) solution. (Upper panel) Cardioplegic solution at 5°C was administered with hypothermia (group 1). (Lower panel) Cardioplegic solution at 37°C was administered without hypothermia (group 2). (= $p < 0.05$ versus before.)*

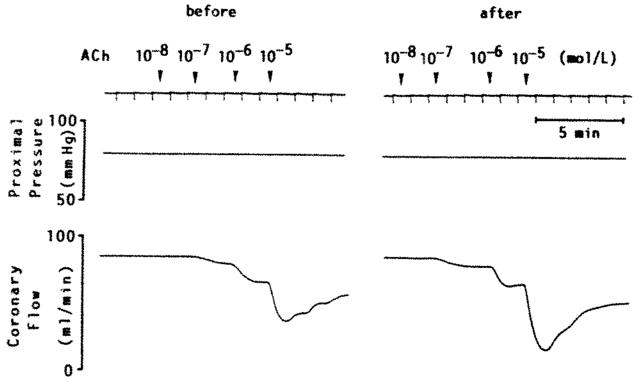

Fig 3. Representative tracings of coronary flow reduction induced by acetylcholine chloride in group 1. Left panel shows the response before the administration of the infusate. Right panel shows the response on rewarming for one hour after the administration of cold cardioplegic solution at 5°C with hypothermia.

Figure 5 summarizes the percent coronary flow reduction induced by acetylcholine (10^{-5} mol/L) when Krebs-Henseleit solution was applied at a temperature of 5°C with hypothermia (group 3) and at 37°C with normothermia (group 4). In group 3, the responses at one, two, and even three hours after cardioplegia administration were significantly augmented compared with the control value (28.1% ± 4.5% during the control period versus 36.1% ± 6.8%, 39.1% ± 5.7%, and 36.1% ± 6.5% at one, two, and three hours after infusion of the solution, respectively). The response at three hours after cardioplegia was significantly increased compared with the value at the same point in group 1. In group 4, there was no significant change in the magnitude of coronary flow reduction induced by acetylcholine throughout the experimental period (23.9% ± 5.4% during the control period, and 25.0% ± 5.0%, 24.9% ± 5.6%, and 24.9% ± 5.8% at one, two, and three hours after infusion of the solution, respectively). No significant difference between groups 2 and 4 was detected in the responses to acetylcholine.

Figure 6 shows dose–response relationships between values before and after cardioplegia with hypothermia (group 1). The dose–response curve shifted upward but not parallel, and the ED_{50} values of each curve were not

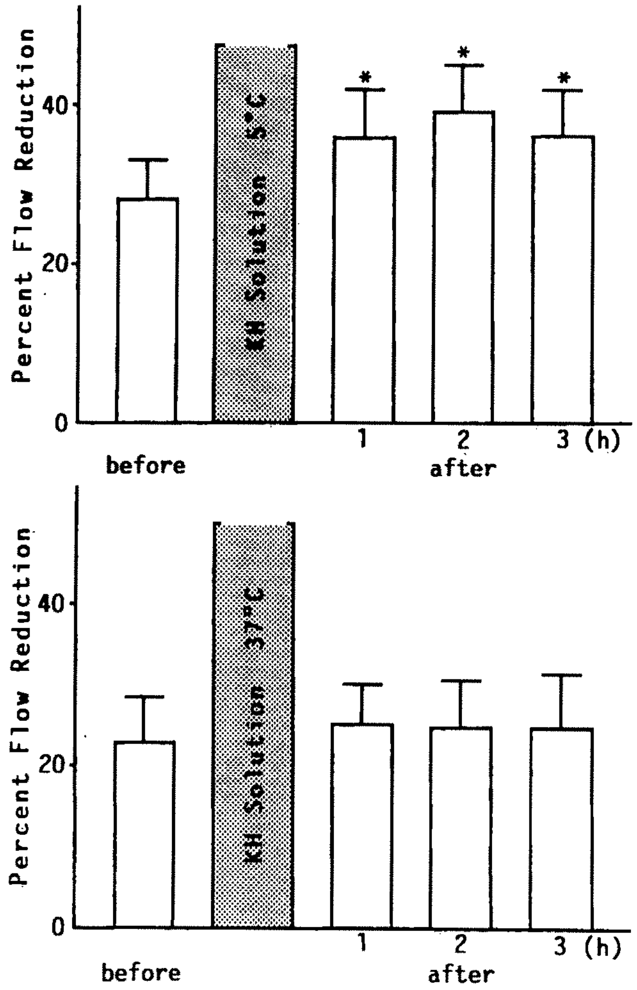

Fig 5. Percent flow reduction induced by acetylcholine chloride (10^{-5} mol/L) before and after the administration of Krebs-Henseleit (KH) solution. (Upper panel) Krebs-Henseleit solution was administered at 5°C with hypothermia (group 3). (Lower panel) Krebs-Henseleit solution was administered at 37°C without hypothermia (group 4). (= p < 0.05 versus before.)*

significantly different before and after cardioplegia: (1.38 ± 0.05) × 10^{-6} mol/L and (1.35 ± 0.02) × 10^{-6} mol/L, respectively.

Responses to Potassium Chloride

Table 1 summarizes the coronary flow reduction induced by potassium chloride (60 mmol/L) before and 1.5 hours after cardioplegia in each group. There were no significant differences in the responses in all four groups.

Comment

There are three salient features of the present study. (1) Vasoconstrictor action of acetylcholine on the pig coronary artery was significantly augmented after the administration of cold cardioplegic solution with hypothermia. (2) A similar phenomenon was seen when cold Krebs-Henseleit solution (5°C) was applied, but was not seen when a warm cardioplegic solution (37°C) was used. (3) The responses to potassium chloride (60 mmol/L) did not change after any of these interventions.

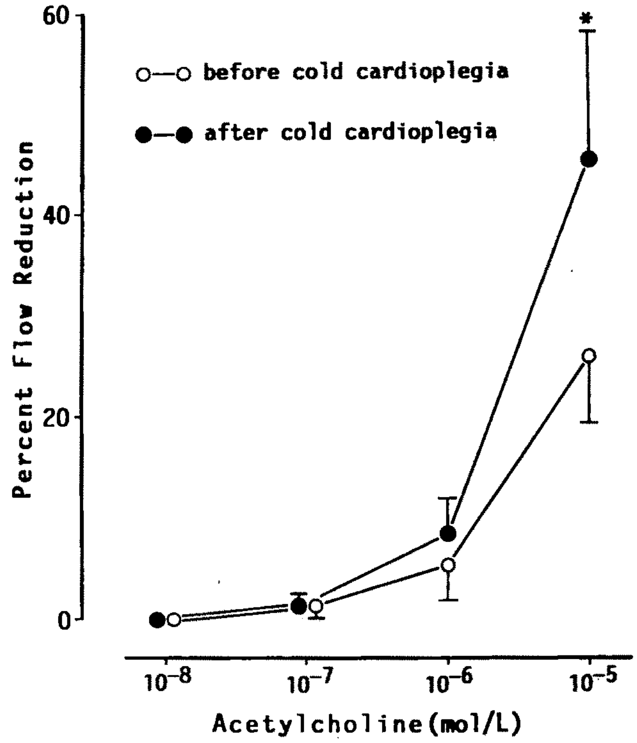

Fig 6. Dose-response relationships to acetylcholine chloride before and one hour after the administration of cold cardioplegic solution at 5°C with hypothermia. (= p < 0.05 versus before at the same concentration.)*

These results suggest that the enhanced vasoconstrictor effects of acetylcholine on the pig coronary artery are due to the lowered temperature. In the present observations, the temperature of the outermost layer of the pig coronary artery decreased to 8°C in five minutes after the initiation of the administration of cold cardioplegic solution or cold Krebs-Henseleit solution and topical cooling, and increased to 37°C in 35 minutes after reperfusion with warm Krebs-Henseleit solution. The augmentation of the coronary response to acetylcholine was demonstrated not in the condition of lowered temperature but in the rewarmed state. Many reports [13–16] have shown that the vasoactive properties of various substances change at low temperature. However, little is known about changes in

Table 1. Percent Flow Reduction by Potassium Chloride (60 mmol/L)[a]

Coronary Infusate	Before	After
Cardioplegic solution, 5°C (group 1, n = 8)	70.8 ± 3.1	70.5 ± 3.8
Cardioplegic solution, 37°C (group 2, n = 8)	60.6 ± 8.1	60.4 ± 6.5
Krebs-Henseleit solution, 5°C (group 3, n = 8)	68.4 ± 7.2	68.4 ± 7.3
Krebs-Henseleit solution, 37°C (group 4, n = 8)	58.6 ± 8.2	56.7 ± 8.3

[a] Data are shown as the mean ± the standard error of the mean.

vascular responsiveness after rewarming as demonstrated in the present study. We have shown the potentiating effect of cooling on the coronary responsiveness to acetylcholine under conditions when the vessel is rewarmed, as is the case in clinical practice.

At present, however, the mechanisms underlying the increased coronary responsiveness to acetylcholine after cooling and subsequent rewarming are not known. Coronary responsiveness to vasoconstrictors seems not to increase generally, as the flow reduction caused by 60 mmol/L of potassium chloride, which contracts vascular smooth muscle by depolarizing the membrane potential, did not significantly change after cooling. It is unlikely that the amount of acetylcholine that reaches and binds to the cholinergic receptor is increased because the activity of acetylcholinesterase, an enzyme to break down acetylcholine, is reported not to be inhibited by low temperature in canine saphenous vein [13, 14].

A possible explanation for the present results is that the augmented coronary contraction by acetylcholine could be derived from changes in the receptor mechanism. Our observation suggests that the affinity of the muscarinic receptor may not increase with cooling, because there were no significant changes in ED_{50} values before and after cooling. However, before we can draw a final conclusion, two questions involving rewarmed vessels have yet to be clarified: whether the number of muscarinic receptors is increased and whether the signal transduction system after receptor activation is changed.

Since the initial work by Furchgott and Zawadzki [17] demonstrating an obligatory role of intimal endothelial cells in the vasodilatory response to acetylcholine, considerable research has been focused on the possible role of endothelial cells in the modulation of vascular responsiveness to various vasoconstrictor agents. Harjula and associates [18] examined the effect of various cardioplegic solutions on the microstructure of endothelial cells in sheep coronary arteries, and reported that cold crystalloid cardioplegia caused disappearance of the endothelial cells and gross deformity of the flow surface. Therefore, another possible explanation is that low temperature per se inhibits the vasodilator action of endothelial cells and augmented the coronary response to acetylcholine in the present study.

The pathogenesis of perioperative coronary spasm is not clear. Increased sympathetic activity, respiratory alkalosis, decreased body temperature, local manipulation of the artery, release of vasoconstrictor substances by platelets, high local concentration of potassium, increased plasma vasopressin levels, and histamine liberation have all been postulated as causes for perioperative coronary spasm [6, 7, 19, 20]. Intracoronary administration of acetylcholine has been reported to provoke an extensive contraction of the coronary artery in patients with variant angina, suggesting that the activation of the cholinergic nervous system may play an important role in the pathogenesis of coronary spasm [9]. Moreover, some investigators [21–23] have reported that surgical denervation of the cardiac plexus is effective in preventing perioperative coronary spasm in the patient with variant angina associated with coronary stenosis.

It is premature to draw any definite conclusion from the present experiments. However, implicit in the present results is that in the clinical setting, cold crystalloid cardioplegic solution and hypothermia may augment coronary contraction provoked by the activation of the parasympathetic nervous system. In patients with a spastic coronary artery, myocardial ischemia could result.

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Notice From the American Board of Thoracic Surgery

The part I (written) examination will be held at the Hyatt-Regency, Dallas/Fort Worth Airport, Dallas, TX, on January 21, 1990. The closing date for registration is August 1, 1989.

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A candidate applying for admission to the certifying examination must fulfill all the requirements of the board in force at the time the application is received.

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Left Coronary Ostial Stenosis: Comparison With Left Main Coronary Artery Stenosis

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We compared 147 consecutive patients who had left coronary ostial stenosis with 254 consecutive patients who had left main coronary artery stenosis treated with coronary artery bypass grafting. Mean age for the left main group was 61.6 years versus 59.7 years for the left ostial group (p = not significant [NS]). In the left ostial group, 43.5% were female and in the left main group, 12% ($p < 0.005$). Prior myocardial infarction had occurred in 53% of patients with left main stenosis and 36% of patients with left ostial stenosis ($p < 0.005$). There were 2.45 ± 1.00 diseased vessels in the left main group and 1.96 ± 1.09 in the left ostial group ($p < 0.0005$). Seven (3%) of the patients with left main stenosis had no associated coronary disease (greater than 50%) versus 24 (16%) of the left ostial group ($p < 0.005$). The degree of left main stenosis was 90% or more in 28.3% of patients versus 42.8% with equivalent ostial narrowing ($p < 0.01$). Left ventricular function was better in the left ostial group than in the left main group (1.61 ± 0.93 versus 2.02 ± 1.11, respectively; $p < 0.0005$). One-month mortality was 10 patients (3.9%) in the left main group and 8 (5.4%) in the left ostial group (p = NS). Perioperative infarction occurred in 8.6% of patients with left main stenosis and 4.7% of patients with left ostial stenosis (p = NS). Mean follow-up was 6.1 years for the left main group and 5.4 years for the left ostial group. Cumulative survival for the left main group and the left ostial group, respectively, was as follows: 1 year, 94.6% and 91.8% (p = NS); 5 years, 85.6% and 83.1% (p = NS); and 10 years, 74.2% and 66.4% (p = NS). Angina recurred in 38.9% of the patients with left main stenosis and 23.0% of patients with left ostial stenosis ($p < 0.005$). Late myocardial infarction occurred in 9.0% of the left main group and 3.5% of the left ostial group ($p < 0.05$). Although differing in gender distribution and the prevalence of associated coronary artery disease and its sequelae, the survival curves are similar for patients with left coronary ostial stenosis and those with left main coronary stenosis.

(Ann Thorac Surg 1989;47:293–6)

Stenosis of the left coronary ostium is a lesion of the aortic wall that encroaches on the orifice of the left main coronary artery and can, therefore, be separated anatomically from left main coronary artery disease. Although both lesions are atherosclerotic in etiology, there may be differences in ascending aortic and coronary atherosclerosis in terms of causation, rate of progression, and associated disease. In an attempt to learn about these considerations, as well as the influence of coronary artery bypass on survival, we compared two groups of patients having one lesion or the other.

Material and Methods

From 1970 through 1984, 147 patients had coronary artery bypass grafting for left coronary ostial stenosis of 50% or more. We compared this group with 254 consecutive patients having coronary bypass grafting for left main stenosis of 50% or more from 1974 through 1980.

All patients underwent coronary angiography and left ventriculography in the right anterior oblique projection. Wall motion of each of five segments was graded on a scale of 1 to 5, and the grades were summed to give a left ventricular score [1]. Left ventricular function was defined as class 1 (score, 5), class 2 (score, 6 through 10), class 3 (score, 11 through 15), and class 4 (score, greater than 15). Stenosis of the ostia and the coronary arteries was estimated visually as the percentage of luminal cross-sectional area lost and usually was based on a composite of two projections.

Patients were classified as having one-, two-, or three-vessel disease based on the presence of a 50% or greater lesion in one or more of the three major coronary arteries. Bypassable lesions of the posterior descending, obtuse marginal, or posterolateral arteries were considered equivalent to patent artery disease but diagonal artery lesions were not so considered. If the posterior descending artery rose from the circumflex, then a lesion affecting the posterior descending would be classed as one-vessel disease, and a second lesion affecting the posterolateral or obtuse marginal artery would be classed as two-vessel disease if both arteries were bypassable.

Angina was graded by the Canadian Cardiovascular Association Classification [2]. Prior myocardial infarction was diagnosed by a history of infarction or by the presence of Q waves on the electrocardiogram. Diabetes mellitus was diagnosed if the patient was taking insulin or

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Table 1. Patient Variables in the Two Groups[a,b]

Variable	Left Main (n = 254)	Left Ostial (n = 147)	p Value
Mean age (yr)	61.6 ± 10.2	59.7 ± 9.6	NS
Female	30 (11.8)	64 (43.5)	<0.005
Diabetes	19 (7.4)	9 (6.1)	NS
Class 3 or 4 angina	219 (86.2)	126 (85.7)	NS
Prior myocardial infarction	134 (52.7)	53 (36.0)	<0.005
Diseased vessels per patient	2.45 ± 1.00	1.96 ± 1.09	<0.0005
No diseased vessels	7 (2.7)	24 (16.3)	<0.025
Stenosis >90%	72 (28.3)	63 (42.8)	<0.01
Left ventricular function	2.02 ± 1.11	1.61 ± 0.93	<0.0005
Normal function	119 (46.8)	88 (59.8)	<0.05

[a] Where applicable, data are shown as the mean ± the standard error of the mean. [b] Numbers in parentheses are percentages.

NS = not significant.

an oral hypoglycemic medication. Perioperative myocardial infarction was diagnosed by the appearance of a new Q wave on postoperative days 1, 2, or 5 or by the ratio of lactate dehydrogenase isoenzymes 1 and 2 (greater than 1.0) on postoperative days 1 and 2.

Operation was performed with cardiopulmonary bypass using moderate hemodilution, systemic hypothermia to 25° to 28°C, topical hypothermia with ice slush, and intermittent aortic cross-clamping until 1977, when cold blood potassium cardioplegia was introduced.

Patients were followed through 1985 by office visit, contact with the physician, or telephone interview or, if dead, by telephone contact with family or friend.

Results

Mean age for the 254 patients with left main artery stenosis was 61.6 years; for those 147 with ostial stenosis it was 59.7 years (p = not significant [NS]). There were 30 female patients (12%) in the former group and 64 (43.5%) in the latter ($p < 0.005$). The incidence of diabetes was similar in both groups (Table 1). Class 3 or 4 angina was present in 86.2% of patients with left main disease and 85.7% of those with left ostial stenosis. Prior myocardial infarction was noted in 134 (52.7%) of the left main group and 53 (36.0%) of the left ostial group ($p < 0.005$). There were 2.45 ± 1.00 diseased vessels per patient in the former group and 1.96 ± 1.09 in the latter ($p < 0.0005$). Seven patients (2.7%) with left main stenosis had no associated coronary stenosis (greater than 50%), whereas 24 (16.3%) of those with ostial stenosis were so classified ($p < 0.0005$), and the mean of age of these patients (53.3 ± 8.8 years) was significantly less ($p < 0.005$) than that of the other patients. The degree of left main stenosis was 90% or more in 28.3% of the left main group, and 42.8% of the ostial group had equivalent ostial narrowing ($p < 0.01$). Left ventricular function generally was good but was significantly better ($p < 0.0005$) in patients with left ostial disease (see Table 1).

Despite the presence of more diseased vessels in the left main group, the number of grafts per patient was similar in both groups (Table 2). The incidence of perioperative myocardial infarction was also similar in both groups (see Table 2). The 1-month operative mortality was 10 patients (3.9%) in the left main group and 8 (5.4%) in the left ostial group (p = NS).

In the left main group, mean follow-up was 6.1 ± 0.16 years, and 27 patients (11%) were lost to follow-up at a mean of 3.7 ± 0.45 years. In the ostial group, mean follow-up was 5.4 ± 0.28 years, and 8 (5.7%) were lost at a mean of 2.8 ± 0.37 years. Cumulative survival curves are shown in Figure 1. Survival data for the left main and left ostial groups, respectively, were as follows: 1 year, 94.6% ± 1.4% and 91.8% ± 2.3% (p = NS); 5 years, 85.6% ± 2.2% and 83.1% ± 3.3% (p = NS); and 10 years, 74.2% ± 4.8% and 66.4% ± 5.9% (p = NS). Thus, the survival curves are comparable for both groups.

As noted in Table 3, there were 48 total deaths (18.8%) in the left main group and 34 (23.1%) in the left ostial group (p = NS). When all deaths that were clearly noncardiac in cause (cancer, trauma, sepsis) were deleted, there were 29 cardiac-related deaths (11.4%) in the left main group and 26 (17.6%) in the ostial group ($p < 0.05$). When deaths were separated by gender and group, there was the same percentage of male deaths in both groups (see Table 3). Although 6 female patients (20%) in the left main group died of all causes as did 18 (28.1%) in the left ostial group, this was not a significant difference.

Table 2. Operative and Perioperative Events[a,b]

Variable	Left Main (n = 254)	Left Ostial (n = 147)	p Value
Grafts per patient	3.1 ± 0.8	3.0 ± 1.0	NS
Perioperative myocardial infarction	22 (8.6)	7 (4.7)	NS
1-Month mortality	10 (3.9)	8 (5.4)	NS

[a] Where applicable, data are shown as the mean ± the standard error of the mean. [b] Numbers in parentheses are percentages.

NS = not significant.

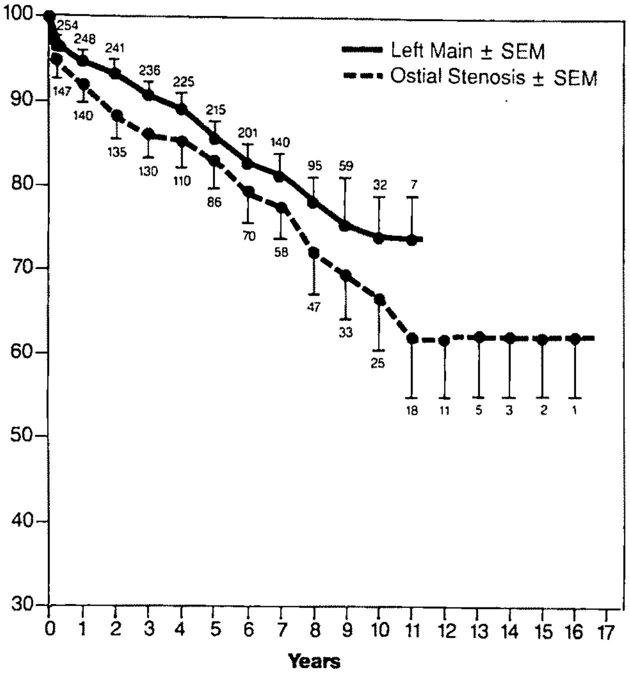

Fig 1. Cumulative survival curves for patients with left main disease and patients with left ostial disease are not significantly different at 1, 5, and 10 years. (SEM = *standard error of the mean.)*

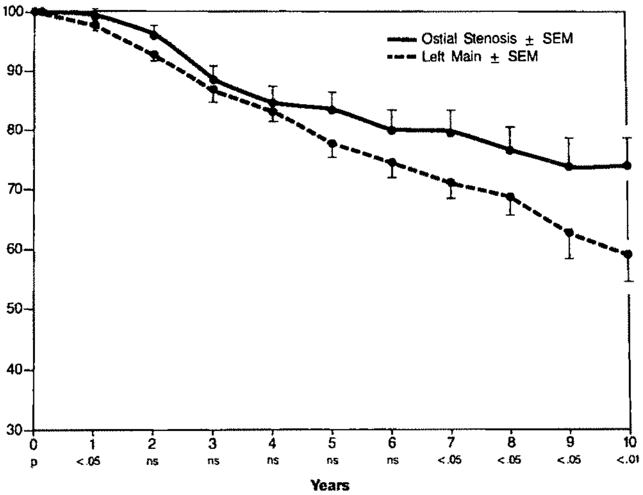

Fig 2. Percentage of patients free of angina after coronary artery bypass grafting for left main and left ostial disease. There is a significant difference (p < *0.05) at years 1, 7, 8, 9, and 10.* (ns = *not significant;* SEM = *standard error of the mean.)*

Angina recurred during follow-up in 95 patients (38.9%) with left main stenosis and 32 (23.0%) with ostial stenosis ($p < 0.005$). On a yearly basis, the incidence of angina recurrence was significantly ($p < 0.05$) greater at years 1, 7, 8, 9, and 10 in those with left main disease (Fig 2). Late myocardial infarction occurred in 22 (9.0%) of those with left main disease and 5 (3.5%) of those with ostial disease ($p < 0.05$). Another revascularization procedure was required in 4.9% of those with left main disease and 2.1% of those with ostial disease (p = NS) (see Table 3).

Comment

Although we believe that all of our patients had atherosclerotic ostial stenosis, there are other uncommon causes of this lesion. These include congenital malformations [3], Takayasu's aortitis [4, 5], syphilis [6], homozygous familial hypercholesterolemia [7, 8], and iatrogenic causes including catheterization [9] or cannulation [10, 11] trauma. During the study period, 3 patients were judged to have both left main and left ostial stenosis, and were not included in this analysis.

Table 3. Angina, Myocardial Infarction, Reoperation, and Death[a]

Variable	Left Main	Left Ostial	p Value
All deaths	48 (18.8)	34 (23.1)	NS
Cardiac-related deaths	29 (11.4)	26 (17.6)	<0.05
All deaths, males	42/224 (18.7)	16/83 (19.2)	NS
All deaths, females	6/30 (20.0)	18/64 (28.1)	NS
Angina	95/244 (38.9)	32/139 (23.0)	<0.005
Myocardial infarction	22/244 (9.0)	5/139 (3.5)	<0.05
Reoperation	12/244 (4.9)	3/139 (2.1)	NS

[a] Numbers in parentheses are percentages.

NS = not significant.

Our total experience with ostial stenosis has been reported [12]. It comprises 41 patients with right, 176 with left, and 11 with bilateral ostial stenosis. Patients with right or bilateral ostial stenosis were not included in the present report, nor were 4 patients with associated aortic valve disease requiring aortic valve replacement. We have not recognized atherosclerosis of the ascending aorta of noteworthy severity or requiring specific treatment or modification of standard approaches such as aortic cannulation, cross-clamping, and vein graft anastomosis in patients with ostial disease.

Our gender distribution in left main stenosis approximates that reported for coronary artery disease generally [13] and left main disease specifically [14]. The greater prevalence of the female gender (43.5%) among patients with left ostial disease in the present study does not attain the equal gender distribution noted in right ostial disease [12]. Female gender was associated with a doubling of operative mortality among patients with left main disease [14] and an equal or greater increase in mortality for all patients having operation for coronary artery disease throughout the study period [13, 15–18]. Thus, it is likely that female gender contributed to the nonsignificant elevation of operative mortality in the ostial group.

Stenosis of 90% or more was associated with increased operative mortality among patients with left main disease [14], and this variable was significantly more prevalent in the ostial group. Left ventricular function was significantly more impaired in the left main group, and is a risk factor for operative mortality among patients with coronary artery disease generally [13] and in left main disease

[14]. In the Coronary Artery Surgery Study [19], women with left main disease and an elevated left ventricular end-diastolic pressure had the highest overall surgical mortality. Although an increasing number of diseased vessels was associated with rising operative mortality from 1970 to 1980 [13], this influence was not manifest in patients with left main disease [14]. The number of grafts performed was similar in both groups and could not account for mortality differences as noted in the early 1970s [13]. Angina class was related to operative mortality among patients with left main disease [14], but this distribution was nearly identical in our two groups.

A recent analysis [20] of operatively treated left main disease in the 1980s revealed that only female gender and emergency operation were associated with increased operative risk, which was 9.1% in 176 patients with a mean age of 65.5 years.

Our only operative approach to left ostial stenosis has been bypass grafting with saphenous vein or internal thoracic artery. We do not believe transaortic endarterectomy is a technically sound approach because of the potential for a distal intimal flap. We have had no experience with patch left ostialplasty, which has its advocates in Europe [21] and may be a preferable approach in the patient with isolated (no associated coronary artery disease) ostial or left main disease. Laser ablation of ostial or left main lesions may be a therapeutic method of the future, but it was not available during the time of this study, and we have had no experience with it.

Our 5-year survival of 85.6% in patients with left main disease is similar to that reported (88.2%) for a slightly earlier period [16], and there are no 10-year data for comparison. Female gender has not been associated with reduced long-term survival in patients with operatively treated coronary artery disease [22–24] or left main disease [20].

The greater incidence of recurrent angina and myocardial infarction in the left main group was likely related to the greater number of diseased vessels in this group. Although the need for reoperation was greater in the left main group, this did not achieve significance.

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Prediction of Post–Cardiopulmonary Bypass Cardiac Output

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The ability to predict cardiac output (CO) before termination of cardiopulmonary bypass (CPB) allows identification of potential complications once the patient is off bypass. We have previously demonstrated that CO early after CPB can be reliably predicted by a plot of venous oxygen saturation at various flow rates on CPB, based on in-line monitoring of venous oxygen saturation. In this study, we evaluated a simplified technique for predicting CO with a series of 50 patients on CPB. When CPB weaning began, patients were normothermic, anesthetized, and paralyzed. Venous oxygen saturation and arterial blood flow were recorded. At low pump flow just before termination of CPB, the final venous oxygen saturation was recorded. Assuming a proportional relationship between venous oxygen saturation and arterial blood flow, CO early after CPB was predicted. The simplified CO prediction was compared with the thermodilution CO immediately after CPB. The simplified technique reliably predicted CO early after CPB compared with the thermodilution technique. The simplicity and reliability increase the clinical value of the CO prediction.

(Ann Thorac Surg 1989;47:297–9)

The separation of patients from cardiopulmonary bypass (CPB) is a very critical stage of cardiac surgical procedures [1, 2]. Many variables currently are used to assess the tolerance for the transition. These include the electrocardiogram, arterial blood pressure, pulmonary pressures, central venous pressure, left atrial pressure, urinary output, direct vision of heart motion and contraction, arterial and venous blood gases, and venous oxygen saturation (SvO_2). Parr and associates [3] reported that cardiac output (CO) is the most reliable predictor of survival after CPB. Therefore, once the decision is made for the termination of CPB, the CO immediately after CPB is one of the most reliable measurements of cardiac function [4–6].

We [1] have previously shown that the thermodilution CO after CPB can be predicted by plotting mixed SvO_2 at various bypass flow rates. In the present study, we simplified the procedure, so that only two measurements of SvO_2 are needed to predict CO after CPB.

Material and Methods

Fifty nonselected adult patients undergoing cardiac surgical procedures utilizing CPB form the basis of this report. The procedures included coronary artery bypass grafting in 35 patients, aortic valve replacement in 2, mitral valve replacement in 6, mitral annuloplasty in 3, aortic valve replacement and mitral valve replacement in 2, closure of an atrial septal defect in 1, and cardiac transplantation in 1.

A Swan-Ganz thermodilution catheter was inserted in all patients for thermodilution CO measurement with the Edwards cardiac output computer (Edwards Laboratories, Santa Ana, CA). All patients were fully anesthetized and paralyzed. Cardiopulmonary bypass was instituted, and patients were immediately cooled to temperatures ranging from 25° to 30°C. An aortic cross-clamp was placed on the ascending aorta proximal to the arch vessels and the arterial cannulation site. Myocardial protection was achieved by topical hypothermia and intermittent blood cardioplegia. Any transpulmonary or regurgitant blood flow during the procedure was adequately vented using a left ventricular sump placed through the right superior pulmonary vein into the left ventricle. The rewarming process began soon before release of the aortic cross-clamp. Throughout CPB, SvO_2 was continuously monitored using the Bentley Oxysat meter (American Bentley, Irvine, CA) incorporated in the venous line of the extracorporeal circuit.

When the patient's temperature was returned to normal (esophageal temperature greater than 37°C and bladder temperature greater than 34°C), weaning from CPB was begun. When weaning was initiated, SvO_2 and arterial blood flow (Q) were recorded. With cardiac variables such as electrocardiographic rhythm, heart rate, volume, and vascular tone carefully monitored, the CPB weaning process was carried out in a stepwise procedure based on the estimated optimal flow (cardiac index = 2.2 L/min/m^2), ie, ¾ Q, ½ Q, ¼ Q, ⅛ Q. At low pump flow just before CPB termination (400 to 700 mL/min), the final SvO_2 was recorded.

The CO early after CPB was then predicted by a

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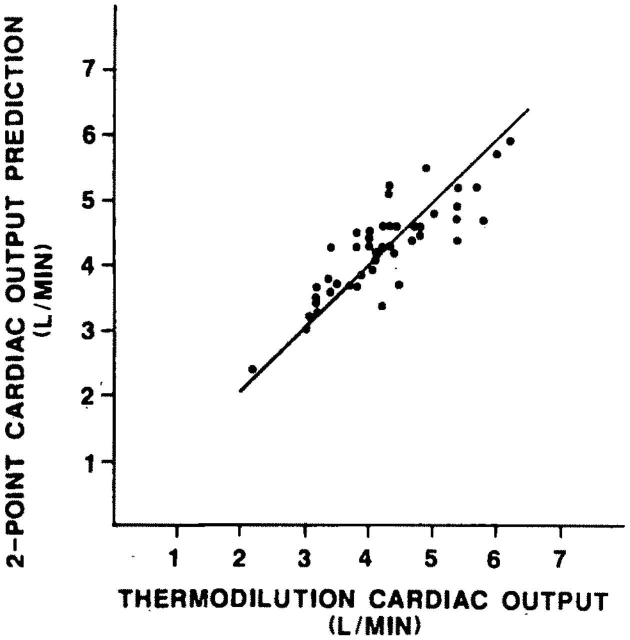

Fig 1. The correlation between the 2-point cardiac output prediction and the thermodilution cardiac output. Correlation and regression analysis showed the following values: r = 0.85 *and* p = 0.0001.

simplified technique (2-point CO prediction) in which the CO prediction assumed a proportional relationship and a 1:1 ratio between SvO_2 and Q with the following equation:

$$SvO_2(1)/Q(1) = SvO_2(2)/Q(2),$$

where $SvO_2(1)$ = venous oxygen saturation when CPB weaning began, Q(1) = arterial blood flow when CPB weaning began, $SvO_2(2)$ = venous oxygen saturation at low flow, and Q(2) = arterial blood flow at low flow. Therefore,

$$Q(2) = (SvO_2[2] \times Q[1])/SvO_2(1).$$

The thermodilution CO immediately after CPB was obtained by an anesthesiologist who was not informed of the CO predictions. The thermodilution CO was determined by the average of three serial CO values. Correlation and regression analysis were used to compare the 2-point CO prediction values with the thermodilution CO values.

Results

In Figure 1, the 2-point CO prediction was plotted against the thermodilution CO. Correlation and regression analysis showed values of $r = 0.85$ and $p = 0.0001$.

Comment

Boyd and co-workers [2] reported that the CO requirement of a patient at any given time is accurately reflected by the arteriovenous oxygen difference calculated with SvO_2. Subsequent investigations [7–10] suggested that either central venous or mixed SvO_2 was an adequate measure of cardiac function. De La Rocha and associates [8] studied SvO_2 and concluded that serial determinations of SvO_2 can be used as a guide in estimating CO. Our group [1] demonstrated that CO can be reliably predicted before CPB termination by using in-line venous oxygen saturation ($r = 0.82$ and $p = 0.0001$).

The common causes of decreased SvO_2 are anemia, low CO, arterial oxygen desaturation, and increased oxygen consumption (Vo_2) [1, 2]. The relationships are summarized in the oxygen consumption equation:

$$Vo_2 = CO \times \text{hemoglobin} \times 13.8 \times (SaO_2 - SvO_2),$$

where SaO_2 = arterial oxygen saturation. Weaning from CPB is of such short duration that oxygen consumption, hemoglobin, and arterial oxygen saturation can be assumed unchanged. The remaining variables—SvO_2 and CO—are linearly related [1, 2, 4, 8, 11, 12]. Hence,

$$Q(2) = (SvO_2[2] \times Q[1])/SvO_2(1).$$

The 2-point CO prediction technique was found to correlate well with the thermodilution CO. Because the thermodilution CO measurement has an inherent 10% error, the 15% error introduced by the 2-point CO prediction is nearly as reliable.

The CO prediction provides an indication of the hemodynamic status of the patient to be separated from CPB. With volume and vascular tone at optimal levels, inadequate circulation is identified by a low CO prediction (cardiac index less than 1.5 $L/min/m^2$). In our institution, full bypass flow (cardiac index = 2.0 to 3.0 $L/min/m^2$) is reinstituted for an additional 15 to 30 minutes when the CO prediction is low, and pharmacological therapy is indicated. A low CO prediction on the second CPB weaning attempt indicates mechanical support is necessary (ie, intraaortic balloon pump, left ventricular assist device).

In addition to circulatory function, pulmonary complications have been identified by the CO prediction. These complications include equipment malfunction (ie, ruptured ventilator tubing), noncardiogenic fulminant pulmonary edema, endotracheal tube shift, and a mucous plug in the mainstem bronchus. A steady decline in SvO_2 and a low CO prediction during termination of CPB can be indicative of such a complication, which necessitates maintenance of CPB until correction is instituted.

With familiarity with the CO prediction principle, estimation of CO can easily be accomplished by observing trends in the SvO_2 changes. In our experience, no patient has had to be returned to CPB within the immediate 15 to 30 minutes after termination after safe separation was indicated by the CO prediction.

In conclusion, utilizing in-line SvO_2 monitoring and the simplified technique, CO early after CPB can be predicted by a basic calculation of the relationship between SvO_2 and Q. The simplicity and reliability increase the clinical value of the CO prediction, and the prediction should be included as a vital variable for safe CPB separation.

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Homograft Aortic Root Replacement to Correct Infective Endocarditis Requiring Seven Open Cardiac Procedures

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Infective endocarditis, presumably from a septic dental focus, affecting the aortic valve was seen as acute aortic regurgitation in a 20-year-old woman. Seven open cardiac procedures for replacement of the aortic valve and left ventricular outflow tract were performed over the subsequent 6 years. Aortic root replacement using a fresh antibiotic-sterilized homograft was performed as the last definitive operative procedure. This article is presented to highlight (1) the use of homograft aortic root replacement for extensive involvement of aortic valve and left ventricular outflow tract in cases of infective endocarditis and (2) the feasibility of multiple sternal reentries when indicated.

(Ann Thorac Surg 1989;47:300–1)

Prosthetic aortic valve replacement for infective endocarditis was described in 1965 [1]. However, prosthetic mechanical valves have their own failings in serving as foci of infection and contributing to wear and tear of normal surrounding tissues [2]. As a result, tissue destruction from prosthetic valve endocarditis is extensive and makes surgical treatment very difficult. Often, a patient with endocarditis affecting implanted valves will require one or more corrective open heart surgical procedures. With each successive operative procedure, there is greater distortion of normal anatomy [3] and hence escalation of potential risk from operation. Corrective operation in these difficult reoperations for prosthetic valve endocarditis should aim to be curative, radical, and safe. We present this case of a young patient who required seven open cardiac surgical procedures before definitive correction of prosthetic valve endocarditis.

This 26-year-old female patient was referred from a distant rural center to the Cardiothoracic Surgical Unit of St. Vincent's Hospital, Sydney, with a malfunctioning prosthetic aortic valve. Six years before this, she was first seen with acute streptococcal endocarditis affecting the aortic root and valve, manifesting as severe aortic regurgitation. The gravity of her condition necessitated prompt surgical intervention at another center. At that time, she had evidence of cardiomegaly, functional tricuspid regurgitation, and pericardial effusion. At operation, a prominent abscess was found in the region of aortic-mitral continuity with complete destruction of the noncoronary cusp of the aortic valve. The abscess cavity was curetted and drained, and the aortic valve excised. The resulting defect was closed in the region of aortic-mitral continuity with a Dacron patch. A 21-mm Björk–Shiley (ABC) prosthesis was used to replace the aortic valve. The patient was asymptomatic for 8 months after operation. Thereafter, prosthetic and left ventricular outflow patch dehiscence, which again was seen as aortic regurgitation, developed. The patient was operated on at that stage, with excision and replacement of the prosthetic patch and valve. Subsequently, she underwent four open cardiac surgical procedures for prosthetic valvular and left ventricular outflow tract dysfunction over the next 3 years. Details of the various operative procedures she underwent are outlined in Table 1.

Six years after her first open heart operation, she was seen at our unit with persisting paravalvular aortic regurgitation and hemolytic anemia. Failure of the previous procedures and her noninfective state prompted consideration of the use of a Bentall procedure. Bearing in mind the problems arising from prosthetic materials in this case, a homograft aortic root replacement was performed, along with reimplantation of both coronary ostia. The freshly prepared, antibiotic-sterilized aortic root homograft was harvested from the recipient heart of a transplant patient in the unit. At operation, the heart was mobilized with some difficulty. Dissection was most tedious in the region of the aorta. Cardiopulmonary bypass was instituted using the femoral artery and bicaval cannulation of the right atrium. The postoperative period was uneventful and the patient was discharged eight days after the operation. An echocardiogram before discharge showed normal function of the newly implanted aortic valve and the left ventricle.

Comment

Prosthetic valve replacement for infective endocarditis was reported in 1965 by Wallace and associates [1]. Since then, it has been accepted as a standard mode of treatment [4–7]. However, the nature of the valve used as replacement also seems to affect the outcome: mechanical

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Table 1. Operative Procedures Performed

No.	Date of Operation	Indication	Procedure	Prosthesis
1	4/82	AVE	AVR + repair of LVOT	21-mm BS + Dacron patch
2	12/82	PD	AVR + repair of LVOT	21-mm BS + Dacron patch
3	4/83	PD	AVR + repair of LVOT	21-mm SJM + Dacron patch
4	5/83	PD	AVR + repair of LVOT	21-mm SJM + Dacron patch
5	9/83	MI + PD	AVR, repair of LVOT + CABG	21-mm SJM + Dacron patch + RSV
6	9/85	PD	Ventriculotomy + repair	. . .
7	9/85	PO bleed	Right thoracotomy	Evacuation of clot
8	3/88	PD + hemolysis	Bentall	Homograft AR

AR = aortic root; AVE = aortic valve endocarditis; AVR = aortic valve replacement; BS = Björk–Shiley; CABG = coronary artery bypass grafts; LVOT = left ventricular outflow tract; MI = myocardial ischemia; PD = prosthetic dehiscence; PO = postoperative; RSV = reversed saphenous vein; SJM = St. Jude Medical.

valves have the highest rate of dehiscence and infection, homograft valves the least [2]. Bioprosthetic valves seem to have an intermediate risk. Prosthetic valve endocarditis in the region of the aortic valve can cause extensive damage to the left ventricular outflow tract along with aortic root abscess formation [2]. Homograft aortic root replacement for prosthetic valve endocarditis associated with aortic root involvement is an accepted and established procedure [8].

Fortunately, our patient withstood the first six procedures with no significant myocardial damage. However, the failure of the procedure after the second operation suggested that all was not well with the technique used. Probably, the extensive nature of tissue destruction contributed to the failure of the primary procedure. Earlier use of the Bentall procedure [9] with the use of an aortic root homograft replacement [8] should therefore have been contemplated.

Gross distortion of aortic and surrounding tissues was evident, necessitating femoral cannulation. Repeat sternotomies can be performed with care and attention to meticulous dissection of the heart and surrounding structures [3, 10, 11].

We thank Barrie Sullivan and her colleagues of the library at St. Vincent's Hospital.

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Annuloplastic Reconstruction for Common Atrioventricular Valvular Regurgitation in Right Isomerism

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Two patients who had common atrioventricular valvular regurgitation associated with right isomerism, univentricular heart of the right ventricular type, transposition of the great arteries, pulmonary stenosis, and both systemic and pulmonary venous anomalies underwent common atrioventricular valvular annuloplasty. They also underwent bilateral, bidirectional cavopulmonary shunt. A Carpentier's ring was used in patient 1 and a polytetrafluoroethylene tube was used in patient 2 to reduce the diameter of the common atrioventricular annuli. Postoperative catheterization confirmed complete elimination of regurgitation of the common atrioventricular valve in both patients.

(Ann Thorac Surg 1989;47:302–4)

Since introduction of the Fontan operation for tricuspid atresia in 1971, numerous attempts to employ this procedure for other complex cardiac defects have been reported. However, postoperative evaluation has disclosed that patients with a univentricular heart of the right ventricular type, common atrioventricular (AV) valve, and systemic and pulmonary venous anomalies are not considered to be good candidates for this type of operation. The purpose of this report is to describe the surgical features of 2 patients in whom common AV valvular repair and cavopulmonary shunt were performed.

Two patients, a 12-year-old boy and a 9-year-old boy, each had a univentricular heart of the right ventricular type, a common atrium, transposition of the great artery, severe pulmonary stenosis, common AV valve, bilateral superior vena cava, total anomalous pulmonary venous connection, and right isomerism. The second patient had previously undergone a left Blalock-Taussig shunt procedure. The cardiothoracic ratio was 0.67 in patient 1 and 0.62 in patient 2. Ventriculography confirmed moderate AV valvular regurgitation and reduced ventricular contraction in both patients. Cardiac catheterization data are shown in Table 1. At operation, the common AV valve consisted of four leaflets, and the annular diameter was 60 mm in patient 1 and 55 mm in patient 2. Repair included common AV valve annuloplasty and end-to-side cavopulmonary anastomosis bilaterally. The Blalock shunt of patient 2 was ligated. In patient 1, a Carpentier's ring (size 36M) was used (Fig 1, left), but the ring was too rigid and did not have a suitable shape for use as a common AV annulus. Therefore, in patient 2, a polytetrafluoroethylene tube (Gore-Tex, 3 mm in diameter) was used to reduce the annular diameter to 35 mm (Fig 1, right). To avoid heart block, 1-cm portions of the annulus at the anterior and the posterior pole were spared from stitches (Fig 2). The postoperative course was uneventful in patient 1. In patient 2, the arterial saturation ratio of oxygen decreased to 64.5% and the atretic pulmonary valve was incised on the next day. The hypoxemia did not improve, however, so the Blalock shunt was reopened and the left pulmonary artery was ligated at the portion between the Blalock shunt and the left cavopulmonary shunt. The postoperative arterial saturation ratio of oxygen was 82% in patient 1 and 86% in patient 2; the cardiothoracic ratio was reduced to 0.49 and 0.54, respectively. Both patients maintained sinus rhythm. Postoperative catheterization confirmed a complete elimination of AV valvular regurgitation in both patients (Fig 3).

Comment

The common AV valve has been regarded as one of the basic conditions of a univentricular heart of the right ventricular type associated with right isomerism. The natural history of these hearts after the occurrence of common AV valvular regurgitation is considered to be disastrous [1, 2]. Most of these patients are not considered to be good candidates for the modified Fontan operation because the Fontan-Choussat criteria exclude those with anomalous systemic as well as pulmonary venous return, with regurgitation of the common AV valve, and with deteriorated ventricular function. Operative mortality has been high, between 50% and 75% [3, 4]. The results of

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Table 1. Cardiac Catheterization Data

	Patient 1		Patient 2	
	Preoperative	Postoperative	Preoperative	Postoperative
SVC pressure (mm Hg)	8	20	6	16
Atrial pressure (mm Hg)	8	6	5	2
IVC pressure (M) (mm Hg)	8	6	5	2
PA pressure (S/D, M) (mm Hg)	20/10, 15	...	15/10, 10	18/12, 11
Ventricular pressure (S/ED) (mm Hg)	120/12	120/5	91/8	110/7
Aortic pressure (S/D, M) (mm Hg)	116/88, 96	108/70, 87	105/72, 65	100/64, 81
Arterial oxygen saturation (%)	68.3	82	87	85.7

D = diastolic; ED = endodiastolic; IVC = inferior vena caval; M = mean; PA = pulmonary arterial; S = systolic; SVC = superior vena caval.

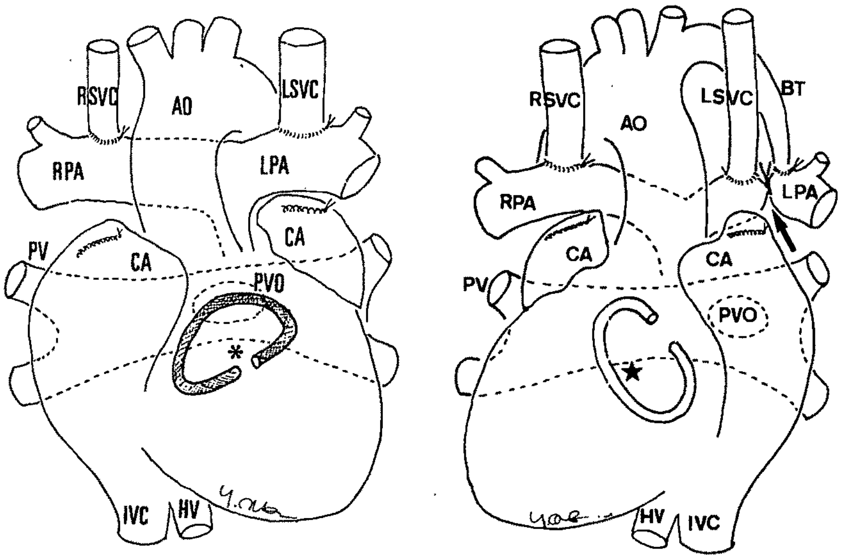

Fig 1. The surgical procedures of patient 1 (left) and patient 2 (right). (AO = *aorta;* BT = *Blalock-Taussig shunt;* CA = *common atrium;* HV = *hepatic vein;* LPA = *left pulmonary artery;* LSVC = *left superior vena cava;* PV = *pulmonary vein;* PVO = *orifice of pulmonary vein;* RPA = *right pulmonary artery;* RSVC = *right superior vena cava;* **Carpentier's ring;* *★expanded polytetrafluoroethylene tube;* arrow = *ligation of the left pulmonary artery.)*

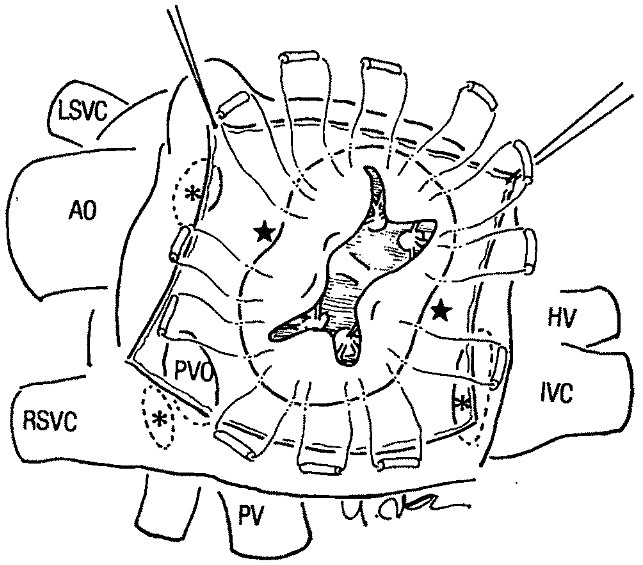

Fig 2. Surgeon's view of the atriotomy in patient 1. (AO = *aorta;* HV = *hepatic vein;* LSVC = *left superior vena cava;* PV = *pulmonary vein;* PVO = *orifice of pulmonary vein;* RSVC = *right superior vena cava;* **orifices of systemic veins;* *★portions of the annulus spared from annuloplasty stitches.)*

various palliative procedures for these patients have not been good [5].

The anatomical features of the common AV valve associated with atrial isomerism were described by Smallhorn and associates [6]. Because of the intrinsic structural weakness of the common AV valve, the condition of the patients who have a univentricular heart and common AV valve tends to deteriorate once regurgitation of the common AV valve develops. Kuroda and colleagues [5] reported that right univentricular hearts gained little muscle mass after systemic–pulmonary shunt, compared with left univentricular hearts. Consequently, regurgitation of the common AV valve occurs more frequently and earlier in right univentricular hearts.

One of the advantages of our procedure is that these hearts may evolve into Fontan-type circulation, as a staged shunt, when the ventricular function improves and pulmonary vascular resistance decreases. The physiological rationale for bidirectional cavopulmonary shunt was described by Hopkins and associates [7]. Among their 12 patients who underwent bidirectional cavopulmonary shunt, 5 patients had a subsequent Fontan-type operation, with good results. The cavopulmonary shunt, as well as the Fontan operation, is considered to be a

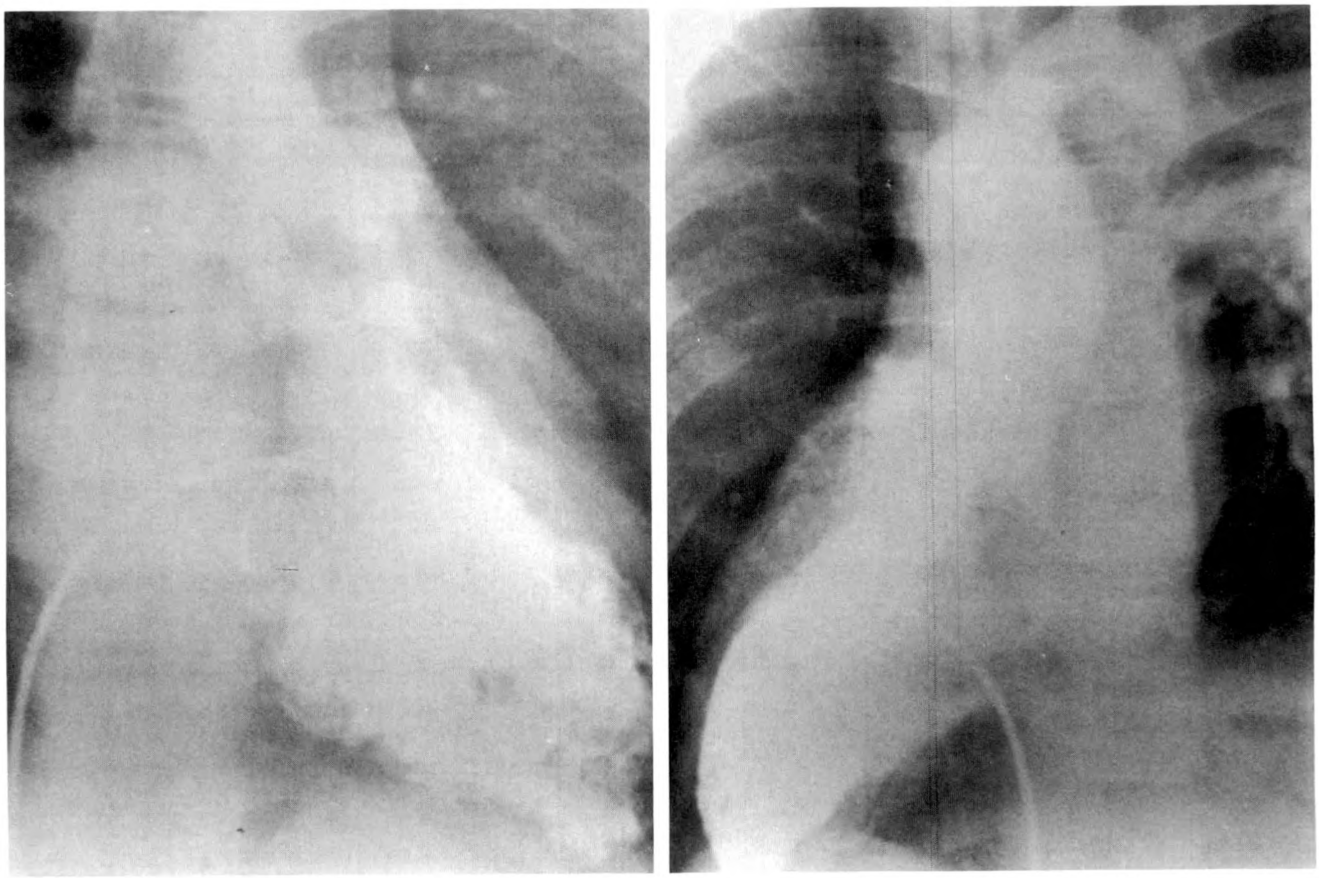

Fig 3. Postoperative ventriculograms of patient 1 (left) and patient 2 (right).

prerequisite procedure for repairing a regurgitant common AV valve because these anastomoses divert venous blood directly to pulmonary circulation and consequently reduce the ventricular preload.

The intolerable postoperative hypoxemia of patient 2 was attributed partly to a high pulmonary vascular resistance resulting from a large Blalock shunt, and partly to an absolute deficiency of the transvalvular pulmonary blood flow.

One of the problems in this operation is conduction disturbance caused by surgical stitches. Usually in a right univentricular heart the AV node is located near the cardiac crux, rarely at the anterior portion of the valvular annulus [8]. We successfully prevent heart block by sparing the most vulnerable portions of the valvular annulus, such as the posterior and anterior central area.

Addendum

Recently, we successfully performed annuloplasty of the common AV valve with a Gore-Tex tube and bidirectional cavopulmonary shunts in an 11-year-old girl.

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Pleuropulmonary Actinomycosis Associated With a Systemic-to-Pulmonary Artery Fistula and Contralateral Metastatic Back Mass

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We report a case of systemic-to-pulmonary artery fistula associated with thoracic actinomycosis and with metastatic hematogenous dissemination to the soft tissues of the back. The difficulty in diagnosing thoracic actinomycosis may predispose to the increased incidence of hematogenous spread of this disease. Although resection of pulmonary tissue including the infectious mass was required in previous cases, resection of the pleural mass alone was curative in this patient when combined with penicillin therapy.

(Ann Thorac Surg 1989;47:305–7)

Fistulas between the systemic and pulmonary circulations are usually congenital. Acquired fistulas may be secondary to trauma, neoplasia, or infection. We have found 5 reported cases due to infection: *Actinomyces* species in four [1–4] and *Blastomyces dermatitidis* in one [5]. We report a fifth case due to actinomycosis that was associated with a metastatic soft tissue abscess of the back.

A 26-year-old man was admitted to the Los Angeles County Harbor/UCLA Medical Center with the chief complaint of left shoulder pain for 3 months. Five months previously he was evaluated for right pleuritic chest pain at another hospital with negative results. Subsequently night sweats and anorexia developed, and the patient lost 30 pounds and was easily fatigued.

On physical examination his temperature was 99°F and he had an ill-defined soft mass, 15 cm in diameter, overlying the left scapula, which was very warm. He was unable to raise his left arm above the level of the shoulder due to pain. He had a carious right lower second premolar. Auscultation of the precordium disclosed a grade III/VI continuous murmur, loudest in the right second intercostal space parasternally. The white blood cell count was 10,200/μL and a chest roentgenogram showed an anterior right paramediastinal mass 12 cm in greatest diameter.

Needle aspiration of the back mass yielded fibrous connective tissue. Arteriography revealed the left subclavian artery and its branches to be normal. However, selective injection of the right internal mammary artery showed it to be 8 mm at its origin (Fig 1A) and filling a vascular network that promptly drained into the right pulmonary artery (Fig 1B). A magnetic resonant imaging scan demonstrated the back mass to be underneath the trapezius muscle and the paramediastinal mass to be abutting the right pericardial surface anteriorly, extending from the second to the fifth rib (Fig 2).

At biopsy of the back mass a necrotic cavity was entered beneath the trapezius fascia. Frozen section revealed only "acute and chronic inflammation"; however, permanent sections demonstrated "sulfur granules" composed of filamentous gram-positive bacteria, characteristic of *Actinomyces*. The patient was treated with 18 million units per day of intravenous penicillin and the back abscess was widely drained. Two weeks after penicillin administration was begun, computed tomography of the chest showed no resolution of the paramediastinal mass. Exploration through a right anterolateral thoracotomy in the third interspace revealed a pleural mass that could be dissected from the chest wall and mediastinum after ligation of the right internal mammary artery. The mass was completely resected without sacrificing lung parenchyma using electrocautery for the numerous small vascular communications. A thrill that was present initially was no longer palpable after resection. Histological examination of the specimen disclosed sulfur granules. The patient received intravenous penicillin for a total of 6 weeks and oral penicillin for an additional year. At 26 months postoperatively he was well.

Comment

Thoracic involvement occurs in 15% to 54% of cases of actinomycosis [6, 7]. The organism is believed to gain access to the lung by aspiration of oral secretions, particularly in patients with poor dental hygiene [2, 7]. The infection progresses slowly with the development of nonspecific symptoms such as night sweats, anorexia, easy fatigability, and weight loss. Sputum cultures are nondiagnostic for pulmonary infections because of the high incidence of *Actinomyces* found in the bronchial

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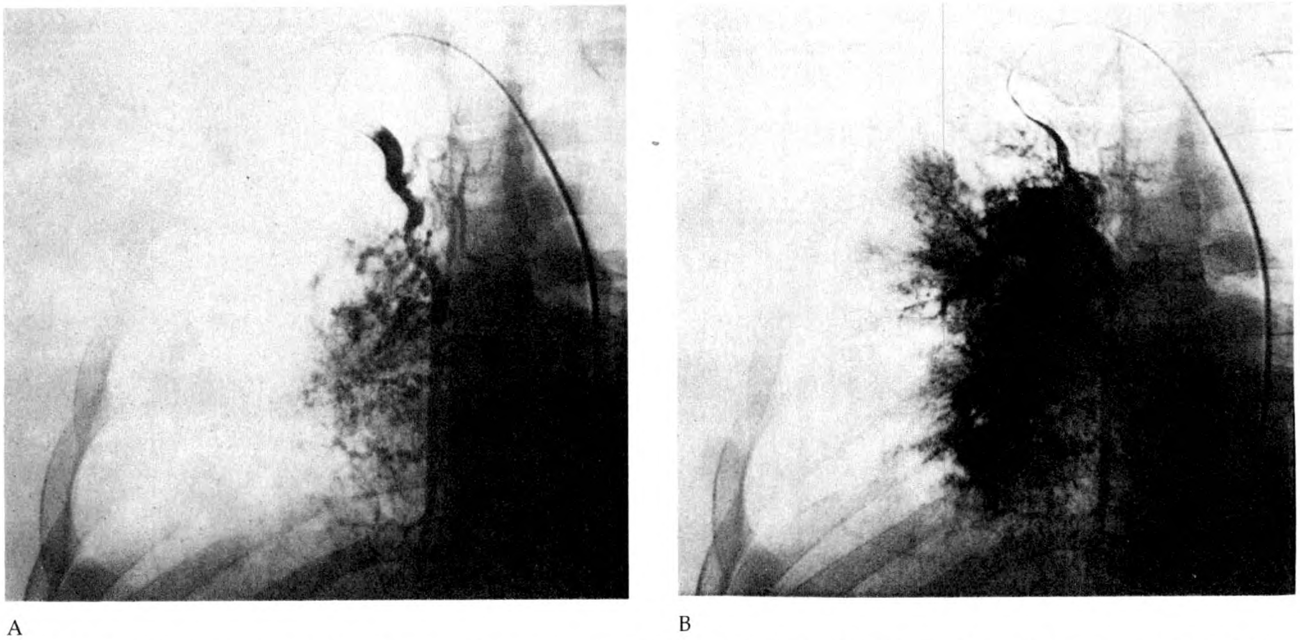

Fig 1. A. A selective injection into the right internal mammary artery showing early filling of the prominent vascular network overlying right pulmonary hilum. B. Later stage of right internal mammary artery injection shows filling of the right pulmonary artery.

washings of patients with chronic bronchopulmonary infections [8]. Draining sinus tracts facilitate the diagnosis of thoracic *Actinomyces* infections when present [7]. In their absence exploratory thoracotomy is usually required to make the diagnosis [7]. In this case, even though the diagnosis was made by biopsy of the back mass, an exploratory thoracotomy was required for diagnosis and resection of the thoracic mass.

Although hematogenous distant dissemination of actinomycosis to soft tissue is considered uncommon in other forms of the disease, it occurs in 42% to 50% of cases of thoracic actinomycosis [9, 10]. The difficulty and delay in diagnosis is felt to be responsible, in part, for this increased incidence of hematogenous dissemination in thoracic infections.

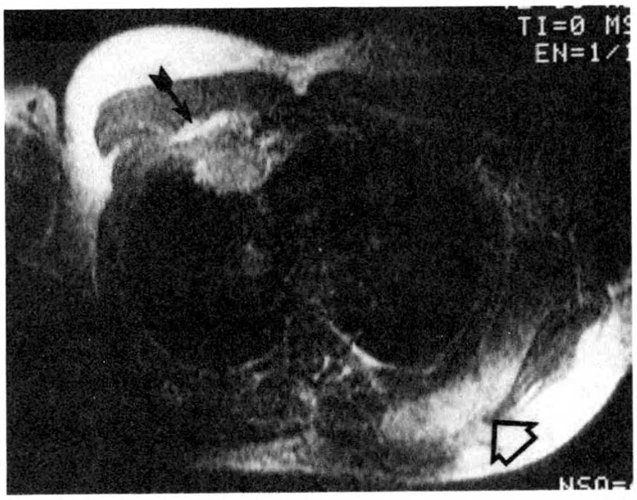

Fig 2. A preoperative nuclear magnetic resonance scan demonstrating the solid right anterior paramediastinal mass (solid black arrow) *and the solid mass underlying the left trapezius muscle* (open black arrow).

Actinomyces grows by direct extension without respect for tissue planes. Pulmonary infection may progress to involve pleura, ribs, sternum, and skin. Extension into a systemic arterial bed may result in a systemic-to-pulmonary artery fistula. Reported cases have involved the intercostal arteries [2, 3], the internal mammary and bronchial arteries [4], and the splenic, renal, and parietal arteries [1].

Surgical ablation of the systemic-to-pulmonary artery connection has required ligation of the systemic artery and resection of the involved lung with all extrapulmonary extension [1]. Lobectomy or segmental resection may be sufficient [4]; however, extensive pulmonary involvement may require pneumonectomy [3]. In our patient, resection of the pleural mass alone was required. Treatment must include high-dose intravenous penicillin. Although the exact dose and duration of antibiotic treatment is controversial, a minimum course of 2 to 3 months has been recommended [11]. We elected to treat our patient for 1 year because of the hematogenous dissemination [10]. Tetracycline may be used in patients allergic to penicillin.

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REVIEW OF RECENT BOOKS

Endoscopic Laser Surgery Handbook
Edited by Stanley M. Shapshay
New York, Marcel Dekker, 1987
520 pp, illustrated, $125

Reviewed by Alphonse Jeanneret, MD, and André Duranceau, MD

This book begins with a large section on basic laser physics and on the interaction of lasers with tissues. The author has made an effort to present simply and comprehensively the basis for laser use without falling into abstract concepts that are more familiar to mathematicians than to surgeons. Despite this approach the 131-page "introduction" to the subject requires time and concentration, especially for the neophyte. It is an excellent base in a consultation and reference book. Understanding the physics and interaction with soft tissues is essential for good comprehension of treatment by laser. The section that follows is a good, concise, and practical review of surgical lasers and delivery systems.

Three chapters cover laser treatment in ear, nose, and throat surgery, and they are followed by three more on laser use on the tracheobronchial tree. They contain detailed explanations of the procedures, their dangers, and the tricks of the trade. However, where this applies, one can only wonder about the absence of comparisons with other treatments already in use for a number of years, such as radiotherapy and cryotherapy. If laser therapy does not change the natural history of a given condition, then it should be compared with other modalities of treatment as objectively as possible. A fourth chapter (chapter 18) on the tracheobronchial tree reviews the indications for and the use of lasers in pediatrics.

In covering the effects and use of lasers on the alimentary tract, one cannot challenge the major advantages of being able to remove a neoplastic obstruction of the esophagus or the colon. Similarly, controlling acute hemorrhage of the upper and lower digestive tract by using this modality may represent a major advantage. When, however, it is suggested, looking at the potential of lasers, that "gastroenterologists will vaporize metastatic tumor deposits in the liver or in the peritoneal cavity through a fiberoptic laparoscope" or that "cholecystectomy will be carried out by laser laparoscopy" while reducing morbidity and mortality, a note of caution is in order. The advantages of these treatments will always have to be compared with established treatment modalities according to how they influence the evolution of disease.

Good perspectives are given on laser use in gynecology, urology, and orthopedics. The background of in vitro and in vivo studies is reviewed for laser use in cardiovascular surgery. It is normal that a section on dynamic phototherapy using porphyrin derivatives be added to this text. Both chapters 8 and 17 emphasize the largely experimental use of the technique. The therapy behind the application of, the possibilities of, and the drawbacks inherent to this approach are well described. The chapter on complications of laser therapy is essential.

In summary, this text is concise and complete, and it should be available in the library of any physician using lasers for therapy.

Montreal, Quebec, Canada

Successful Management of Aberrant Subclavian Artery–Esophageal Fistula in an Infant

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This report describes a 4-month-old female infant with complex congenital heart disease and prolonged nasogastric intubation who developed an aberrant subclavian artery–esophageal fistula that was successfully managed in a two-staged procedure. To our knowledge, this is the first patient to survive correction of this problem after massive hemorrhage.

(Ann Thorac Surg 1989;47:308–9)

In all previous reports of aberrant subclavian artery–esophageal fistulas, death has occurred either as a result of hemorrhage or in the immediate postoperative period after attempts to correct the problem [1, 2]. The patient described here represents, to our knowledge, the first successful management of an aberrant subclavian artery–esophageal fistula in an infant.

The patient was a full-term infant with Down's syndrome and congestive heart failure. Cardiac catheterization revealed a posterior ventricular septal defect, a right aortic arch, an anomalous left subclavian artery crossing posterior to the esophagus, a patent left ductus arteriosus, and peripheral pulmonary arterial stenosis.

The patient's congestive heart failure was poorly controlled medically and she was taken to the operating room at 1 month of age for closure of the ventricular septal defect and the atrial septal defect, pulmonary valvuloplasty, and ligation and division of the patent ductus arteriosus. Her postoperative course was complicated by prolonged ventilator support for 1 month and a cardiac arrest due to aspiration of a feeding 6 weeks after operation. A nasogastric tube was in place for gastric decompression or feeding for the entire postoperative period.

Eight weeks after cardiac operation she had an episode of bright red bleeding from the nasogastric tube and from her mouth, which caused hypotension but stopped with iced saline lavage of the stomach. Her blood pressure was stabilized with fluids and one unit of packed red blood cells.

Four hours later she developed recurrent bleeding through the nasogastric tube and from her mouth. Hypotension developed again, and because of continued bleeding the patient was taken immediately to the operating room. She remained hypotensive despite ongoing blood replacement, and because the most likely source of the hemorrhage was thought to be a peptic ulcer or Mallory-Weiss tear, a laparotomy was performed.

At operation, her stomach was distended with blood. A gastrotomy was performed but no source of bleeding was found in the stomach or at the esophagogastric junction. Bright red bleeding was seen emanating from higher in the esophagus, and an arterial-esophageal fistula was considered to be the likely source of the hemorrhage. At this time, the patient became very bradycardic and had no recordable blood pressure. A rapid left thoracotomy was carried out for open cardiac massage. Once hemodynamic stability was restored, it was decided to "exclude" the esophagus by first ligating it just above the diaphragm with two sutures of 0-chromic. Through a right neck incision, the esophagus was mobilized. The distal segment was ligated with a 0-chromic suture and the proximal esophagus was brought out as an end esophagostomy.

The patient remained stable and the gastrotomy was closed. A gastrostomy tube was placed and a pyloroplasty was performed. The abdomen and chest were closed, and the child returned to the intensive care unit. Nine days after the esophagus was excluded, the patient underwent a right thoracotomy, through which a fistula between the aberrant left subclavian artery and the esophagus was identified. The left subclavian artery was ligated at its origin and distal to the fistula. The esophageal opening was sutured closed with 4-0 silk sutures.

Three weeks after the second procedure, the child had a tracheostomy placed. Over the ensuing 3 months the child improved significantly and was receiving the majority of her nutrition via the gastrostomy. She had no ill effects from the subclavian artery ligation and had no recurrence of the fistula or bleeding. Our plan was to reestablish esophageal continuity at 10 months of age. Unfortunately she suffered an arrest from a mucous plug in her tracheostomy and died 14 weeks after closure of the esophagoarterial fistula.

Comment

An aberrant subclavian artery is present in 0.5% of the general population. The artery lies posterior to the esophagus in virtually all cases [3]. Most patients with this condition are asymptomatic. Those with symptoms usually are seen as adults complaining of difficulty swallowing due to compression of the posterior esophagus by the anomalous artery (dysphagia lusoria). Gross is credited with one of the first surgical corrections of dysphagia lusoria by division of the subclavian artery in 1946 [4].

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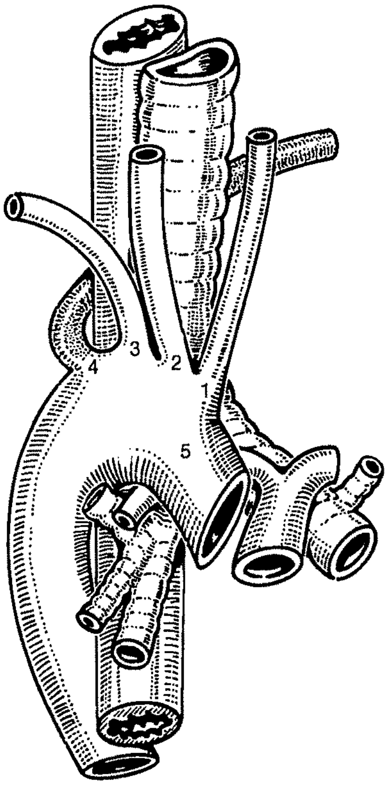

Fig 1. Aberrant left subclavian artery from a right aortic arch. (1) Left common carotid artery. (2) Right common carotid artery. (3) Right subclavian artery. (4) Left subclavian artery. (5) Ascending aorta of right aortic arch. Modified from Molz and Burri [6].

Ectasia of the origin of the right aberrant subclavian artery is known as Kommerell's diverticulum and is usually insignificant. However, at least 1 case of spontaneous arterial–esophageal fistula from such a malformation has been reported [5]. If a patient is suspected to have an aberrant subclavian artery, rigid esophagoscopy will reveal the abnormal posterior pulsation, and the endoscope may be used to compress the vessel and obliterate the pulse in the affected arm as a diagnostic test. The presence of an aberrant subclavian artery should alert one to the possible concurrent anomaly of a nonrecurrent laryngeal nerve.

A right aberrant subclavian artery occurs in 80% of patients with an anomalous subclavian artery. A left aberrant subclavian artery from a right aortic arch (Fig 1), such as in our patient, is the second most common variant, occurring in 12% of patients. The remaining patients have a right aberrant subclavian artery associated with aortic coarctation (5%) or with complete interruption of the aortic arch (3%) [6].

Successful management of a fistula between an aberrant subclavian artery and the esophagus demands prompt recognition of the pathology and control of hemorrhage. A high index of suspicion is warranted in the patient with bright red upper gastrointestinal bleeding who has had any type of firm esophageal tube in place for a prolonged period of time. If possible, the fistula should be tamponaded with a Sengstaken-type device. Fistulas involving the right aberrant subclavian artery should be approached through a left thoracotomy as the anomalous vessel originates distal to the left subclavian artery. Conversely, the more rare aberrant left subclavian artery requires a right thoracotomy because of its origin from the right aortic arch.

When tamponade of the esophagoarterial fistula is unsuccessful, esophageal "exclusion," which has been performed in the past for esophageal perforation [7], can be rapidly performed, controls the hemorrhage, and allows the surgeon to approach the fistula in a stable patient at a later time.

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Vascular Sling With Tracheomalacia: Surgical Management

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Surgical repair of pulmonary artery sling without concomitant correction of associated tracheal abnormalities has yielded poor results in the past. We combined vascular sling repair done during cardiopulmonary bypass through a median sternotomy incision with tracheopexy for severe associated tracheomalacia in 2 infants. Neither experienced substantial postoperative respiratory difficulties and both had patent vascular anastomoses at 1 year after repair, thus supporting this approach when this combination of lesions is present.

(Ann Thorac Surg 1989;47:310–11)

Although vascular repair alone of pulmonary artery sling has successfully relieved respiratory symptoms [1], many patients continue to have obstructive airway symptoms that prolong postoperative recovery and increase operative mortality [2, 3]. Tracheal anomalies occur in about 50% of these cases and include localized tracheomalacia and fixed stenosis from complete tracheal rings [4]. Relief of tracheal obstruction may be difficult when segments of fixed stenosis are present, but may be more easily accomplished in patients with localized tracheomalacia by using techniques to put external traction on the involved segment as have been described for tracheomalacia with tracheoesophageal fistula [5]. We describe 2 infants with vascular sling and tracheomalacia in whom cardiopulmonary bypass was used for vascular repair and then support of the abnormal segment of trachea was achieved by modified aortopexy and tracheopexy.

Patient 1

A 3.36-kg girl with Down's syndrome became cyanotic and dyspneic two hours after birth and required endotracheal intubation. She then improved and was extubated but underwent cardiac catheterization because of a systolic murmur. She was found to have a pulmonary artery sling with a ventricular and atrial septal defect with a pulmonary to systemic blood flow ratio of 2.3:1. She improved on medical therapy and was discharged home. After 1 week, she again had episodes of cyanosis and was readmitted. A chest roentgenogram during a cyanotic spell showed hyperinflation of the left lung.

At 7 weeks of age, operation was performed after bronchoscopy showed marked slit-like narrowing of the distal trachea, carina, and left main stem bronchus. Using a median sternotomy incision and cardiopulmonary bypass, the ductus arteriosus was divided and a small ventricular and atrial septal defect were both closed by direct suture. The left pulmonary artery was detached and dissected from behind the trachea and distally toward the hilum to ensure a nonobstructive course after anastomosis. Anastomosis with the main pulmonary artery was performed using continuous 6-0 PDS suture posteriorly and interrupted 7-0 Prolene (Ethicon, Houston, TX) anteriorly. After discontinuing cardiopulmonary bypass, the distal trachea and carina were exposed and clearly lacked adequate cartilaginous support. As the aorta was directly anterior to the involved airway, the abnormal distal trachea and left mainstem bronchus were first sutured to the adventitia of the posterior aortic wall. Before chest closure, sutures placed in the adventitia of the aorta anteriorly and then to the endothoracic fascia lateral to the sternum were tied, thus placing moderate anterior traction on the abnormal airway. Bronchoscopy immediately after chest closure showed open airways with only minor distortion of the lumen of the left mainstem bronchus.

The patient did well postoperatively, was extubated on the first postoperative day, and had no respiratory difficulties. She was discharged on the 11th postoperative day. Recatheterization at 1.5 years showed an open left pulmonary artery anastomosis with mild stenosis (6 mm Hg gradient). She continues to do well and has no respiratory symptoms.

Patient 2

This patient was admitted at 3 weeks of age with dyspnea and wheezing, treated for pneumonia, and discharged after 6 days. At 6 weeks of age, he had severe respiratory distress with wheezing and fever and was readmitted after resuscitation from a respiratory arrest. Treatment was begun for presumed bronchiolitis, but he deteriorated and required endotracheal intubation. Cardiac catheterization done because of suspected heart disease with pulmonary edema showed pulmonary artery sling and a possible small atrial septal defect. On bronchoscopy there was a narrow distal trachea from external compression and a markedly narrowed left mainstem bronchus. After resolution of his respiratory infection, he was able to be

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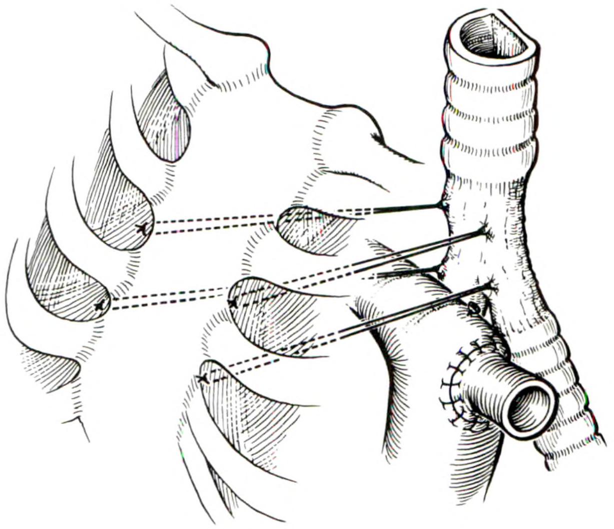

Fig 1. Left anterior oblique view of the establishment of external support of the airway involved with tracheomalacia in patient 2.

weaned from the ventilator, improved, and was discharged from the hospital.

At age 12 weeks he had recurrent pulmonary congestion and cough and then became cyanotic and apneic, and again required resuscitation and endotracheal intubation. At age 13 weeks, he underwent an operation using a median sternotomy and cardiopulmonary bypass. The ductus was divided and no atrial septal defect was found. The mobilization and anastomosis of the left pulmonary artery were done as described for patient 1. As the involved airway did not lie directly behind the aorta but more to the right, we placed four sutures of 5-0 Prolene in the anterior tracheal wall, carina, and proximal left mainstem bronchus, brought these directly through the intercostal spaces lateral to the sternum, and tied them with moderate tension just after sternal closure (Fig 1). Bronchoscopy after chest closure showed an open airway with only mild narrowing of the left mainstem bronchus.

Because of marked fluid retention associated with preoperative paralysis, the patient first underwent diuresis and then was extubated on the fifth postoperative day. He thereafter had normal respiratory function and was discharged on the 13th postoperative day. Cardiac catheterization performed at age 1.5 years showed a normal-sized patent left pulmonary artery anastomosis. He has not had significant respiratory symptoms since his operation.

Comment

Although pulmonary artery sling can be asymptomatic or have early symptoms that later resolve, patients with severe recurrent respiratory compromise such as ours will have a high early mortality without surgical intervention [6]. The dismal results of surgical repair of vascular sling in the past have been due to the poor patency rate of the vascular anastomosis and the persistence of respiratory compromise due to associated tracheal abnormalities. Although the left thoracotomy approach has been preferred by some surgeons [1, 3], a median sternotomy with cardiopulmonary bypass provides better exposure and, we believe, the best conditions to assure a technically perfect vascular anastomosis. Bronchoscopy before repair is essential to determine whether there is fixed stenosis or substantial localized tracheomalacia. Single-stage repair of pulmonary artery sling with tracheal resection for fixed stenosis has been successfully performed and should improve results for this combination of lesions [7]. Localized tracheomalacia can also severely compromise postoperative respiratory function and has been corrected by external support using aortopexy or tracheopexy in 2 cases reported by Campbell and colleagues, 1 done late after repair of pulmonary artery sling and 1 done concomitantly with vascular repair [8].

Our experience supports the use of single-stage repair for pulmonary artery sling using cardiopulmonary bypass for vascular repair and adding external airway support by tracheopexy for major segmental tracheomalacia. Although we performed bronchoscopy before and immediately after chest closure to confirm proper suture placement and effective airway support, with the current availability of a very small fiberoptic endoscope, it would be better to perform the tracheal suspension while visualizing the effect endoscopically. Although we describe our successful experience in only 2 patients using this approach, considering the severity of their preoperative symptoms and bronchoscopic findings, it seems justified to conclude that the tracheal procedure contributed substantially to their freedom from early postoperative respiratory difficulties.

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Transpericardial Bronchial Closure With Omentopexy for Postpneumonectomy Bronchopleural Fistula

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We report a case of successful closure of a postpneumonectomy bronchopleural fistula by means of the transpericardial approach with omentopexy through a median sternotomy incision. This method minimizes problems of infection, healing, and pulmonary function.

(Ann Thorac Surg 1989;47:312–3)

Bronchopleural fistula after pneumonectomy is the most dreaded complication of thoracic operations, because it is difficult to close the stump of a fistula in an infected thoracic cavity and a new fistula tends to occur. We treated a patient with bronchopleural fistula by bronchial division and omentopexy through a median sternotomy. This procedure seems to have some advantages over other procedures.

A 61-year-old man underwent right pneumonectomy at another hospital for bronchiectasia in 1980. After the operation, a bronchopleural fistula developed and the patient underwent open window thoracostomy in 1985. However, the fistula and chronic septic drainage, cultures of which grew *Pseudomonas aeruginosa*, persisted for 2 years. Eventually, the patient was transferred to our hospital. On examination, he was slightly dyspneic. Blood pressure was 112/80 mm Hg, and the pulse was 68 beats per minute and regular. Bronchoscopy and bronchography showed a 1.5-cm residual right main bronchial stump with two large fistulas (Fig 1A). Pulmonary function tests demonstrated a restrictive pattern with a vital capacity of 1.17 L (36.3%) and a forced expiratory volume in 1 second of 0.92 L (78.6%). Arterial blood gas analysis revealed that the oxygen saturation was 98%, the oxygen partial pressure was 97 mm Hg, the carbon dioxide partial pressure was 41 mm Hg, and the pH was 7.42.

Antibiotics were administered preoperatively according to the sensitivities of cultured organisms. On December 2, 1987, the patient underwent operation. A median sternotomy incision extending to the umbilicus was used, with the patient in a supine position, and the pericardium was opened. Tapes were placed around the aorta and superior vena cava and the vessels were retracted. The posterior pericardium was incised and the right pulmonary artery was retracted to the cauda. The lower trachea and right and left bronchi were surrounded by only mild fibrosis and could be fully mobilized. The trachea and right main bronchus were divided by two applications of a stapler (TA-30; United States Surgical Corp, Norwalk, CT) with 4.8-mm staples. The peritoneal cavity was entered through the same incision, and the greater omentum was dissected free from the stomach (along the greater curvature) and from the transverse colon. The left gastroepiploic vessels were tied and cut near the hilum of the spleen. The base of the pedicle contained the right gastroepiploic vessels near the pylorus. The omental flap was brought up through the anterior diaphragm and pericardium and interposed between the new stumps (Fig 2). Several 4-0 Prolene sutures were used to maintain its position. The sternum and the median skin were closed in a routine fashion and dressed. The open right thoracic cavity was irrigated with a large volume of saline solution containing povidone iodine while the patient was maintained in the supine position. The peripheral orifices of the fistulas were scratched. Pedicle flaps of the remaining right major and minor pectoral muscles, divided from the humerus and scapula, respectively, were fixed to fill the right pleural space. The skin was closed around suction drainage tubes.

Tracheotomy and mechanical ventilation were required postoperatively. The thoracotomy wound healed without becoming infected and the patient remains well 6 months later (Fig 1B).

Comment

In 1960 a transpericardial approach to the carina through a left anterior L-shaped incision was reported by Padhi and Lynn [1]. Abruzzini [2] and Perelman and Ambatjello [3] have had the most experience with the reclosure of postpneumonectomy bronchopleural fistulas via the transpericardial approach. This approach has several advantages over the conventional lateral approach through a thoracotomy incision. The thick mediastinal pleura seals off the mediastinal space from the contaminated pleural space, so the operative field is sterile and has relatively unscarred tissue. The main bronchus can be divided without making a blind bronchial pocket. Sternotomy in a supine position, which minimizes muscle damage, is well tolerated from the standpoint of pulmonary function. A stump of at least 10 mm is neccessary to permit secure transpericardial bronchial closure [4]. Baldwin and Mark

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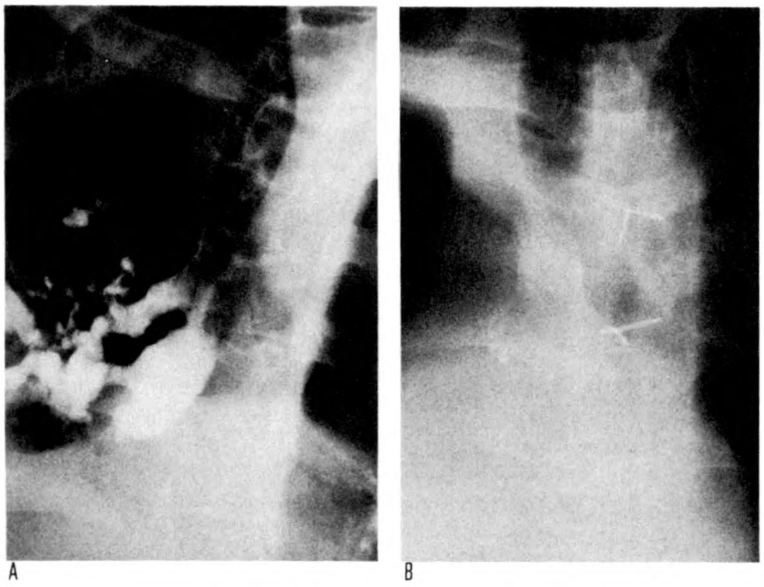

Fig 1. (A) Preoperative bronchogram showing the right residual main bronchus and fistulas. (B) Chest roentgenogram showing the smooth trachea and the left main bronchus after complete closure of the fistula.

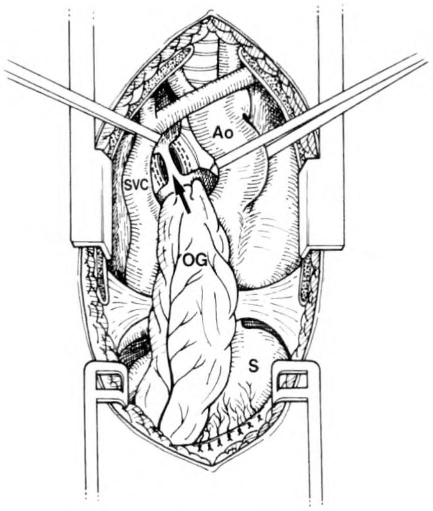

Fig 2. The bronchial stump is divided and closed through the median sternotomy. The pedicled omental flap is brought up and interposed. (Ao = *ascending aorta;* OG = *pedicled omental flap;* S = *stomach;* SVC = *superior vena cava.)*

[4] reported 3 cases of bronchial closure by this approach, but 1 of their patients was found to have a recurrent fistula.

Patterson and colleagues [5] applied omentopexy to the anastomotic site of the trachea through a median sternotomy in double-lung transplantations. We considered that omentopexy could help to prevent recurrence in our patient. The pedicled omental flap provides a highly vascular covering with an ample lymphatic supply and thus provides considerable aid toward repair. It is especially effective in inhibiting intrathoracic infection [5–7]. There are no reports of transpericardial bronchial closure combined with omentopexy for bronchopleural fistula, to the best of our knowledge. Transposition of the omental flap can be easily employed in the same operative field. Omentopexy makes transpericardial bronchial closure secure, and we therefore recommend this technique for postpneumonectomy bronchopleural fistula. Successful fistula closure does not require thoracoplasty [8] in general, but in our patient we performed thoracoplasty with muscle flaps because an open window thoracostomy had previously been performed.

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Percutaneous Endoscopic Tracheostomy

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Bedside percutaneous tracheostomies are increasingly performed. This avoids patient transport to the operating room. Complications of this procedure are largely related to the blind nature of the technique. After laboratory studies, 4 patients underwent percutaneous endoscopic guided tracheostomy in a selective clinical trial. There were no procedure-related complications. Endoscopic guidance ensures precise low tracheostomy position, prevents paratracheal tube misplacement, and avoids inadvertent injuries.

(Ann Thorac Surg 1989;47:314–5)

Surgical tracheostomy continues to be associated with complication rates ranging up to 45% [1–4]. These are in part related to patient management outside the intensive care unit. Scheduling constraints may cause delays in operation, and costs are increased when tracheostomy is performed in the operating room. Ciaglia and colleagues [5] and Toye and colleagues [6] have each separately reported percutaneous tracheostomy techniques. Although these reports have shown the feasibility of bedside percutaneous tracheostomy, new complications characterized by paratracheal tube insertion and immediate tube displacement have been described [6]. Precision and safety of bedside percutaneous tracheostomy may therefore be enhanced with endoscopic guidance.

Material and Methods

The patient is positioned with the interscapular region elevated to facilitate extension of the neck. A flexible fiberoptic bronchoscope is introduced via the endotracheal tube, and the latter is pulled back until the tip is just distal to the larynx. This enables endoscopic guidance and continued ventilation throughout the entire procedure. After transillumination and palpation of the trachea, a small incision is made over the third ring and the platysma is bluntly dissected. A needle catheter is then inserted below the second or third tracheal cartilage. Entry into the airway can be verified endoscopically and by aspiration of air into a syringe attached to the needle catheter. After the syringe is removed, a guidewire is passed through the catheter (Fig 1). A Teflon sleeve is placed over the guidewire to make it more rigid, and the Ciaglia Percutaneous Introducer Set (Cook Inc) is used to progressively dilate the tracheostomy up to 28F to 32F. This allows the introduction of a No. 6 or No. 8 tracheostomy tube (Shiley) over an appropriate dilator of smaller caliber (Fig 2). The airway is established after removal of the guidewire, Teflon sleeve, and dilator.

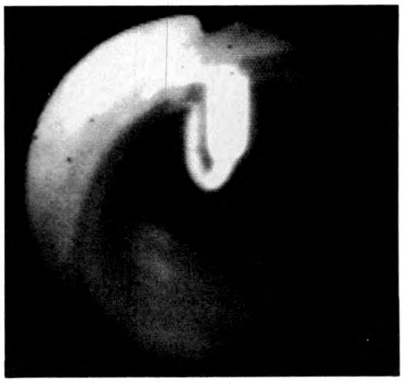

Fig 1. Endoscopic view of the guidewire being threaded through a cannula.

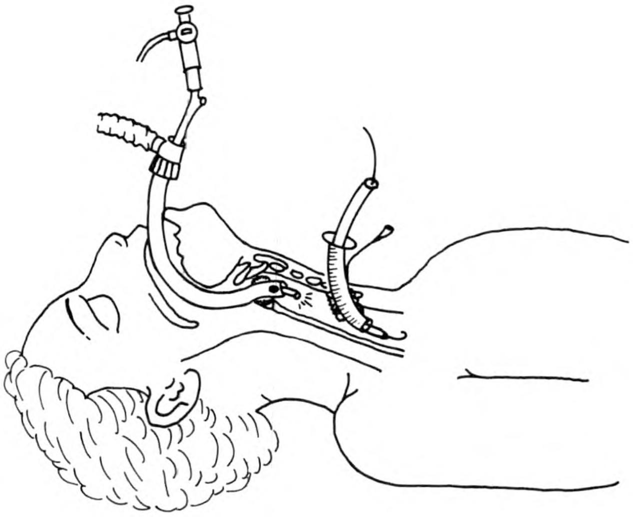

Fig 2. Endoscopic guided placement of a tracheostomy tube and dilator over a previously positioned guidewire.

Comment

The technical feasibility of endoscopic guidance was first tested in 5 dogs. Animals received humane care according

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to NIH guidelines. Placement was achieved within ten minutes and low tracheostomy was precisely carried out using transillumination and palpation. At postmortem examination, damage to the trachea was limited to the tracheostomy site.

Clinically, this procedure was performed electively in 4 patients. This was carried out in the intensive care unit under local anesthesia and mild sedation. These patients had all been mechanically ventilated for 10 to 20 days and required prolonged intubation. In each case, tracheostomy was performed within 10 to 15 minutes, during which time ventilatory support continued. In the fourth patient, endoscopic guidance facilitated identification of a misplaced guidewire and subsequent tube misplacement was avoided. To date, no tracheostomy balloon cuff has broken during insertion. There were no procedure-related complications in a follow-up period up to 46 days. Application of endoscopic guidance can prevent laryngeal damage and injury to the posterior wall of the trachea and esophagus. Furthermore, transillumination can facilitate identification of the tracheal rings in the obese individual. In patients with short necks or enlarged thyroid glands, ultrasound guidance may prove to be a useful adjunct in the future.

These selected cases demonstrate the feasibility and advantage of endoscopic guidance for performance of bedside percutaneous tracheostomy. We believe that in selected patients this method is preferable and cost effective in comparison with standard surgical techniques.

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Cardioplegia Delivery by Combined Aortic Root and Coronary Sinus Perfusion

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Retrograde coronary sinus perfusion for the administration of cardioplegic solutions has recently been the subject of renewed interest. A method is described for the administration of bolus antegrade cardioplegia followed by continuous retrograde coronary sinus perfusion, particularly for patients with left main artery disease, left main equivalent, or aortic root/aortic valve disease. Advantages of the technique are discussed, as well as its limitations and its use for myocardial preservation in heart transplantation.

(Ann Thorac Surg 1989;47:316–7)

Adequate myocardial preservation during open heart operations necessitates rapid cardiac asystole and reduction of myocardial oxygen consumption facilitated by internal and external cooling. External cooling is usually provided by suffusion of cold saline or saline slush, whereas internal cooling is most often provided by the infusion of cold cardioplegic solution containing potassium via the aortic root. The limitations of antegrade cardioplegia in patients with proximal critical coronary artery stenoses or aortic root/aortic valve disease are well documented [1]. Recently, retrograde coronary sinus perfusion, described in 1898 and used clinically in 1956 by Lillehei and associates [2], has been the subject of renewed interest [3]. We describe a method for the combined administration of bolus antegrade cardioplegia followed by continuous retrograde coronary sinus perfusion with cold (4°C) cardioplegic solution.

Median sternotomy, incision of the pericardium, and creation of a pericardial cradle are performed in standard fashion. Arterial cannulation can be via the ascending aorta or, for difficult aortic root/aortic valve pathology, via the common femoral artery. Bicaval cannulation is then performed. For patients undergoing coronary artery bypass grafting, the order of proximal or distal anastomoses is at the surgeon's discretion.

After the institution of cardiopulmonary bypass, a pursestring suture is placed on the ascending aorta and a cardioplegia catheter is introduced. The aortic cross-clamp is applied and cold cardioplegic solution is infused in an antegrade fashion. A bolus of 500 to 1,000 mL is administered to obtain rapid cardiac asystole and myocardial temperature between 10° and 15°C. Simultaneously, cold saline solution or saline slush, or both, is applied topically. The vena cavae are clamped or snared. The arrested heart is then lifted to expose the posterior portion of the atrioventricular groove.

A 1-cm atriotomy is then made in the right atrium at a point 1 cm from the coronary sinus opening, and a commercially available coronary sinus catheter (DPL Coronary Sinus Catheter, DPL, Inc, Grand Rapids, MI) is advanced into the coronary sinus opening using a right angle clamp. Recently we have also been using a catheter containing a stylet for coronary sinus cannulation via a right atrial pursestring suture. This catheter then produces balloon occlusion of the coronary sinus and allows continuous retrograde coronary sinus perfusion to maintain the myocardial temperature around 10°C. One must be careful when the balloon is inflated with 3 mL of saline solution that it does not occlude the opening of the middle cardiac vein (Fig 1).

During retrograde perfusion the coronary sinus pressure is measured via an in-line pressure transducer and maintained below 40 mm Hg by control of the flow rate of the cardioplegic solution. We start with a flow rate of 50 mL/min to maintain myocardial temperature at approximately 10°C. Simultaneously, venting of the left side is accomplished by the aortic root. A schematic representation of the catheter system is shown in Figure 2.

Upon completion of the procedure, the coronary sinus catheter is removed and the small atriotomy is closed using a 4-0 continuous polypropylene suture. Removal of the antegrade cardioplegia catheter and other cannulas proceeds in a standard fashion.

Slight modifications of the technique are required in aortic valvular disease and in aortic root disease. In aortic dissection, where antegrade cardioplegia delivery is not possible, deep systemic hypothermia (20° to 22°C) is utilized. In both aortic dissection and aortic valvular disease, venting via the right superior pulmonary vein is required to obtain adequate exposure to place the retrograde catheter.

We have used this technique in 80 patients and have found that it is most useful in patients with left main disease, left main equivalent, or aortic root/aortic valve disease. It offers several distinct advantages. Delivery of cardioplegic solution is continuous. Myocardial temperature drifts are avoided [4], as is the need for bolus injections of cardioplegic solution after completion of each

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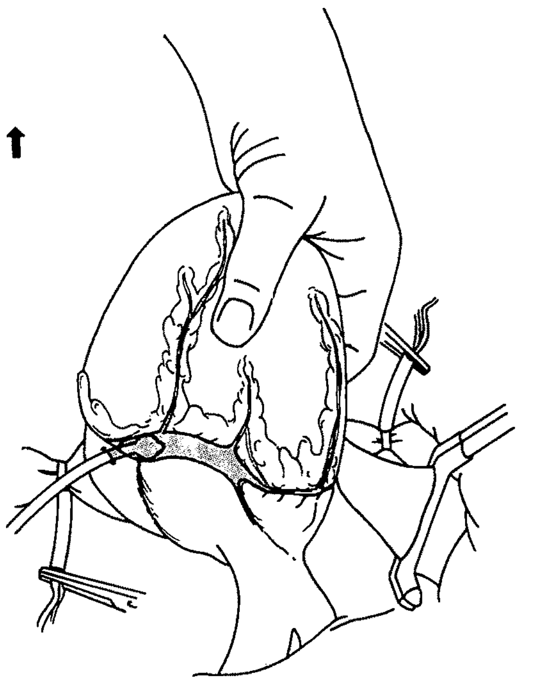

Fig 1. The heart retracted cephalad, exposing the coronary sinus, with the balloon occlusion catheter proximal to the middle cardiac vein.

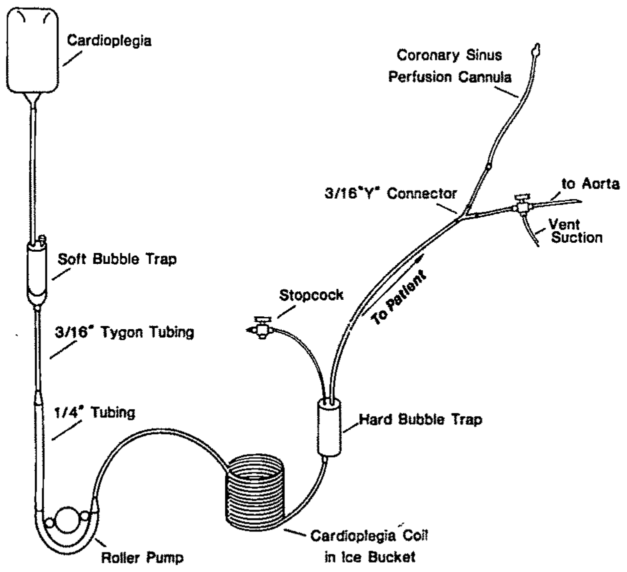

Fig 2. Combined antegrade/retrograde cardioplegia delivery system in use at our institution.

distal anastomosis. The operative field remains dry because of the retrograde perfusion. In addition, in aortic root and aortic valve procedures, there is no need for direct coronary perfusion catheters, and the risk of late ostial stenosis is avoided [5].

An extremely interesting utilization of this technique is in heart transplantation. For myocardial protection during orthotopic heart transplantation the coronary sinus is cannulated after completion of the left atrial anastomosis and continuous cardioplegia is given as described previously. The right atrial, aortic, and pulmonary artery anastomoses are completed. The catheter is then removed after removal of the aortic cross-clamp.

Disadvantages of this technique are few. A right atriotomy and bicaval cannulation are usually required. Concerns regarding damage to the coronary sinus or conduction system have been raised. In the early European trials, when a Foley catheter was used for balloon occlusion, there were several reports of coronary sinus rupture and death. However, since commercially produced coronary sinus catheters have been available this complication has not been reported, and it was not seen in our series. Similarly, the incidence of complete heart block has been negligible in our own series and in European clinical trials. The incidence of atrial or ventricular arrhythmias has not been different than with antegrade cardioplegia.

This method provides excellent myocardial protection for most cardiac procedures. It should be in the repertoire of all cardiac surgeons.

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New Technique for Repair of Ascending Thoracic Aortic Dissections

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Dacron graft replacement of the ascending aorta for thoracic dissections often results in major intraoperative or postoperative hemorrhage due to tissue tearing at the suture lines. We report a promising solution to this problem: strengthening the aortic wall with glutaraldehyde solution. Using this technique, we obtained a tough, resistant tissue that could be sutured without disintegration. We have used the method successfully in 5 consecutive patients.

(Ann Thorac Surg 1989;47:318–9)

Aortic dissection is usually associated with medial necrosis secondary to atherosclerosis or collagen cross-linking deficiencies. This results in a thin, fragile adventitial wall for providing aortic continuity. In the ascending aorta particularly, a weak adventitia, high wall tension, and the absence of reinforcing pleura substantially increase the risk of rupture and justify the emergent surgical replacement of the ascending aorta. However, the tenuous nature of the tissue enhances the possibility of suture line tearing, thereby posing a major operative risk.

Several methods have been proposed to solve this problem, including the use of glue [1], sewing the graft inside the aorta and then wrapping the graft with the remaining tissue [2], decompressing the wrapped aorta, if necessary, by creating an ascending aorta-to-right atrial fistula [3], and inserting a graft with rigid ends inside the aorta and holding the graft in place with external ties [4]. We have found each of these methods unsatisfactory in our hands. We here describe a simple method for toughening the aorta by direct application of 25% glutaraldehyde solution to the aortic wall in vivo. Glutaraldehyde has been used for many years in cardiac operations, although, so far, its two major applications have been limited to stabilization of porcine heart valves and autologous or xenologous pericardial patches.

Methods and Results

After median sternotomy the pericardium is exposed, but not opened, to contain any thrombus that may have sealed an adventitial tear. A femoral artery is exposed and cannulated after heparinization. The pericardium is then opened, a right atrial cannula is inserted, cardiopulmonary bypass is started, and the patient is cooled to 17°C. The aorta is clamped just proximal to the innominate artery and, depending on the entry site, resected from approximately 1 cm distal to the coronary ostia to 1 cm proximal to the clamp. A sponge is placed in the left ventricle, the field is walled off with sponges, and the coronary ostia are blocked by perfusion cannulas or cotton applicators. The left ventricular vent is turned off and the field is kept dry with wall suction. Cotton balls that have been soaked in 25% glutaraldehyde solution (Edward Laboratories, Irvine, CA) are then placed inside and outside of the proximal and distal ends of the aorta and between the intimal and adventitial layers for seven minutes (Fig 1). The cotton balls are then removed and the aorta is rinsed with saline, avoiding any contact with the extracorporeal circulation. The aortic valve is then replaced or resuspended if necessary.

The treated adventitia and media become noticeably thicker and tougher during and after treatment. The texture of the "tanned" aorta is resistant to tearing and handles sutures well. The posterior aspect of the proximal suture line is constructed first with interrupted mattress sutures (2-0 Prolene with a tapered SH needle) placed through the graft, aortic wall, and Teflon strips that were also soaked in glutaraldehyde solution. A second layer is run, over and over, with a continuous suture. The arch vessels are then clamped, the pump is turned off, and the aorta is unclamped. The posterior aspect of the distal anastomosis is constructed next using the same technique. After this, the anterior portion of the distal anastomosis is similarly constructed except that a running mattress suture is used for the first layer. The pump is then turned on, air is evacuated from the aorta, the arch vessels are unclamped, the aorta is reclamped, and the anterior aspect of the proximal anastomosis is completed in similar fashion to the anterior aspect of the distal anastomosis. This sequence allows accurate placement of sutures in the area of the left coronary artery without the graft obstructing vision and permits access to the coronary ostia for cardioplegia administration throughout the operation.

Five consecutive patients have been operated on successfully using this technique. After removal of the cross-clamp, we have never had to place additional sutures to control bleeding, and bleeding was not a problem either intraoperatively or postoperatively. All patients were discharged from the hospital. The longest follow-up has been 24 months. During this time we have detected no

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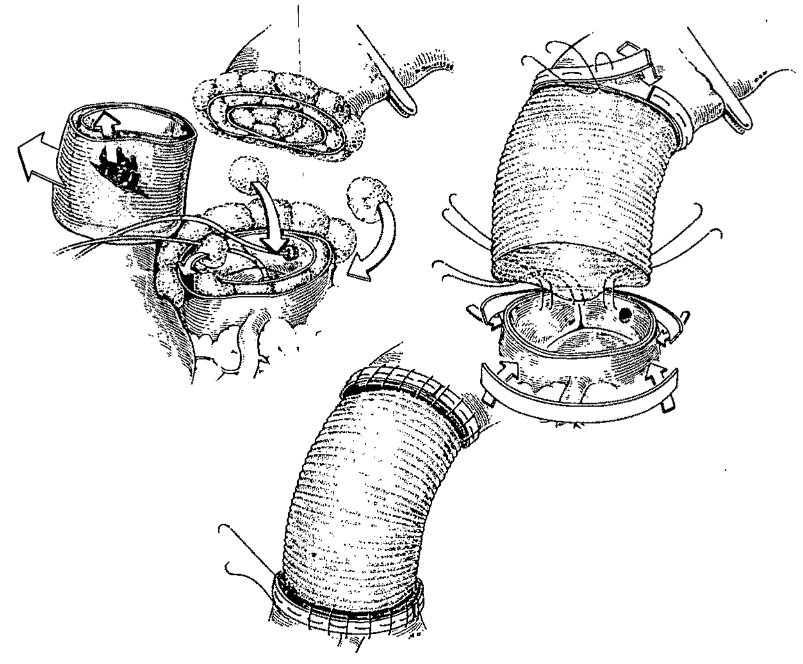

Fig 1. The use of glutaraldehyde-soaked cotton balls when operating on type A thoracic dissections. It is essential that the bowl on the instrument table containing the glutaraldehyde solution be clearly identified and that the coronary ostia be well protected during placement of the cotton balls.

long-term problem with the use of glutaraldehyde based on either clinical or chest roentgenographic findings. One patient died 1 year postoperatively of congestive heart failure and myocardial infarction; a postmortem examination was not performed. One patient died 4 months postoperatively of myocardial infarction. A postmortem examination showed well healed suture lines to the graft, no aneurysm formation proximal or distal to the graft, and no calcification in the treated portions of the aorta. Histological sections of the treated portions of the aorta were indistinguishable from sections of untreated aorta.

Comment

Glutaraldehyde-protein interactions are incompletely understood, although there is probably some cross-linking of lysine residues. We carried out experimental studies with canine aorta treated in similar fashion and found that the glutaraldehyde-treated aorta had less elasticity than normal aorta, but was not inelastic when compared with Dacron. The loss of elasticity in glutaraldehyde-treated aorta was approximately 50%. No histological difference was apparent in treated and untreated aorta. The seven-minute application time was based on laboratory experiments [5]. The high concentration of glutaraldehyde that we used (25% vs. 0.625% for porcine valve storage) was based on experiments with canine aorta that showed no acute deleterious effect, the short contact time between glutaraldehyde and aorta, and the critical load-bearing nature of the tissues. Glutaraldehyde treatment probably prevents bleeding by maintaining some of the elastic properties of the aorta and by toughening the tissue so that tears do not propagate once the aorta has been unclamped. There is also a theoretical secondary advantage in that cross-linking may decrease the possibility of recurrent aneurysm formation of the remaining proximal aorta.

The potential complications of this technique are calcification [6] of the treated aorta and toxicity secondary to contamination of the pump or surrounding tissue by the glutaraldehyde. In our experience, toxicity is easily avoided by careful use of the product and walling off of adjacent tissues. If calcification is to be a problem, it should not develop for several years, based on the experience with glutaraldehyde-treated porcine valves [7]. We assume that a short fixation time, no storage time, the relatively nonmoving nature of the structure, and the autologous origin of the tissue will decrease this risk.

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A Method of Applying Fibrin Sealant Using an Atomizing Needle

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A needle modification is described that enables fibrin sealant to be applied as a fine spray to the operative site. The techniques for modification and use of the needle are presented.

(Ann Thorac Surg 1989;47:320)

The application of fibrin sealant to achieve hemostasis is very useful in cardiac operations. Application of this sealant to suture lines on the heart has been extremely successful in sealing these areas and achieving hemostasis [1–4].

We have recently developed an atomizing needle that enables fibrin sealant to be applied in a fine layer over a wide area. This application method has proven particularly effective in controlling bleeding in extensive areas such as those resulting from dissection during reoperations.

Fibrin sealant is applied as a two component system. The first component consists of a mixture of calcium chloride and topical thrombin. The second component is cryoprecipitate. We currently use the following formula:

Syringe No. 1: 500 mg of $CaCl_2$ plus 25,000 units of thrombin powder (USP thrombostat) with sufficient sterile saline to produce 50 mL.
Syringe No. 2: 50 mL of cryoprecipitate.

The atomizing needles are made by altering the tip of any 21-gauge disposable metal needle as shown in Figure 1. To accomplish this, the needle tip is pressed lightly against a flat metal object such as the blunt end of a forceps (Fig 2). This modification causes the stream of sealant to atomize as it passes through the tip of the needle, resulting in a fine spray. Alternatively, preformed needles (Popper & Sons, Inc, New Hyde Park, NY) are commercially available.

The spraying action of the needle is then tested by injecting saline through it. If the angle of the tip is too acute, the spray will resemble a "V" and be poorly dispersed. In that case the tip must be straightened slightly. If the spraying action does not occur, the tip must be bent to a greater degree.

The syringes are positioned so that the two sealant component sprays overlap when applied. This results in a fine, viscous coating of fibrin sealant (Fig 3). Immediate hemostasis is generally achieved. We have found this technique to be very useful.

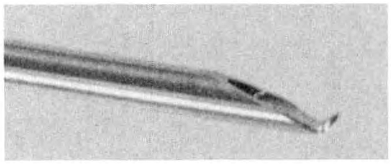

Fig 1. Needle tip modification.

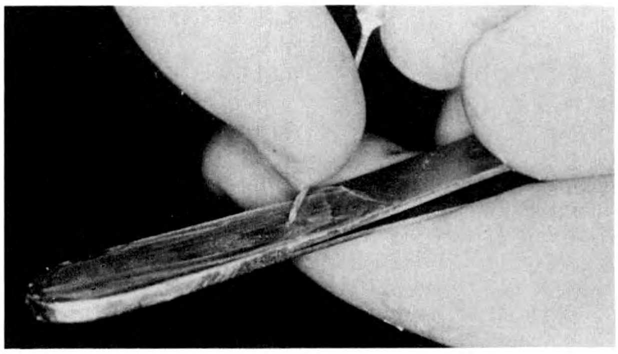

Fig 2. Method of needle modification.

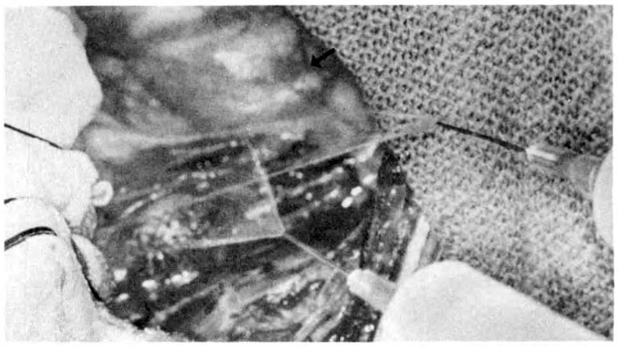

Fig 3. Spray application of fibrin sealant components. Note the fine, uniform layer of fibrin sealant that is produced (arrow).

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Open Heart Surgery in Infancy

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Periodically, articles appear in the literature that either dramatically change the treatment of a specific disease or excite the interest of the readers to question why an entire field has not moved forward at a faster pace. An article that I remember quite well was written by Herbert Sloan, MD, and associates and appeared in *The Journal of Thoracic and Cardiovascular Surgery* in October of 1962 [1]. The article presented a broad approach to being able to perform operations in small infants and children of low body weight.

The concept of miniaturizing the oxygenator, tubing cannula, and other equipment (Fig 1) was well presented by the authors. I remember the techniques and concepts well because they influenced me to become interested in the more routine operations for correction of congenital heart defects in infants. In looking back at the article 27 years later, one is constantly reminded of the basic concept that small infants, usually younger than 2 years of age, were operated on only as a last resort. Thus, when one analyzes the mortality, which is higher than one would anticipate in 1989, it is obvious that a large cause of the mortality in this trend-setting article was most likely related to the fact that the patients were only operated on when all other methods of treatment failed. The improvements were reported as most dramatic in infants with ventricular septal defect, malnutrition, and severe heart failure. The perfusion techniques presented by the authors were very similiar to ones that I, myself, used throughout the majority of my career for correcting defects in small infants. This was essentially continuous cardiopulmonary bypass with hypothermia, with flow being reduced, if needed, during the important part of the intracardiac repair.

During the 1960s, considerable efforts were expended on animal research to reduce body temperature and accomplish total circulatory arrest. These longer periods of arrest were associated with reduced success. Sloan and associates, however, emphasized a more practical approach for visibility during the operation. Intermittent aortic occlusion, which still has remained a very viable technique when performed for short periods, was used to improve intracardiac exposure. It was mentioned that during the more difficult operations, the esophageal temperature was lowered to 20°C instead of 28° or 30°C. At this temperature, brief periods of complete interruption of the circulation were possible. These shorter periods of circulatory arrest have remained attractive as, in general, shorter periods of ischemia usually mean less morbidity and mortality.

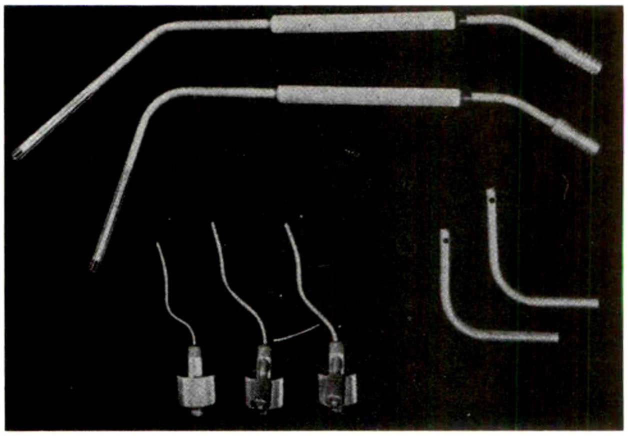

Fig 1. Arterial cannulas, venous cannulas, and small aspirating tips for perfusion in infants. Reprinted from [1] by permission of The C.V. Mosby Co.

Clearly this was a paper reflecting pioneering work in the field of repair of congenital heart defects. It was printed well before operations in 4- and 5-kg patients with extracorporeal circulation were routinely considered. In fact, it was many years after this publication before the same results were attainable by many institutions around the world. Certainly today when we see extremely low mortality numbers addressed to complex repairs in neonates, it is of interest to look to the past and see where the major breakthroughs were accomplished.

The results of the paper, per se, were not as dramatic as the attention to the details of the perfusion techniques and the recognition that the basic physiology of the neonate was well understood by the authors. Obviously, others would follow with improved mortality and a wider spectrum of operations in subsequent years. However, this manuscript clearly should be regarded as one of the hallmarks of originality in the history of congenital heart surgery.

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Ventricular Aneurysm due to Blunt Chest Injury

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A left ventricular aneurysm developed in 3 patients sustaining blunt chest injury. Evidence of an acute myocardial infarction on the electrocardiogram and enzyme analysis prompted cardiac catheterization, which revealed total occlusion of the left anterior descending coronary artery in 2 of the 3 patients. Ventricular aneurysmectomy was performed in each patient. A review of the literature revealed 32 previously reported patients with left ventricular aneurysm caused by blunt trauma. Clinical features, catheterization or autopsy findings, and outcome are examined.

(Ann Thorac Surg 1989;47:322–9)

The usual etiological process of left ventricular aneurysm is a myocardial infarction due to coronary artery disease. Much less frequently, aneurysm formation is secondary to a blunt chest injury. Regardless of the etiology, the complications associated with left ventricular aneurysm remain potentially life-threatening.

Traumatic left ventricular aneurysm (TLVA) following nonpenetrating chest injury was diagnosed and managed in 3 patients at Loyola University Medical Center in recent years. The case histories of these patients and a review of the world literature concerning this entity form the basis of this report. Within the literature review, we examine the relationship between injury to the left anterior descending coronary artery (LAD) and the development of ventricular aneurysm formation.

Case Reports

Patient 1

A 44-year-old man sustained blunt chest trauma during a bicycle collision, when the handlebars of one of the bicycles struck his chest. He was seen at Loyola University Medical Center 18 days later with complaints of shortness of breath during minimal exertion, persistent pleuritic chest pain, and substernal soreness.

The patient had undergone aortic valve replacement with a Starr–Edwards valve 8 years previously for congenital aortic stenosis with angina. Two years later, he experienced transient blindness secondary to thromboembolism despite therapeutic anticoagulation. Replacement of the aortic prosthesis with a 23-mm Björk-Shiley prosthesis was performed. Subsequently, the patient had done quite well and had shown excellent exercise tolerance (New York Heart Association functional class I).

Assessment on admission revealed a blood pressure of 112/85 mm Hg (without paradox) and a heart rate of 70 beats per minute. No jugular venous distention was noted. The point of maximal impulse was located in the fifth intercostal space in the anterior axillary line. A crisp prosthetic aortic second sound was present. A grade 2/4 early systolic murmur was auscultated. There were no diastolic murmurs. Tenderness was present over the midportion of the sternum. Examination was otherwise normal.

The electrocardiogram (ECG) revealed the presence of first-degree atrioventricular block and left bundle-branch block. A chest roentgenogram revealed cardiomegaly and a retrosternal density. Sternal tomography confirmed an undisplaced fracture of the midportion of the sternum.

Investigation of recent decompensation in cardiac function included fluoroscopy of the aortic prosthesis, which appeared normal. A radionuclide cardiac scan revealed a left ventricular ejection fraction of 24%, with substantial apical dyskinesia and anterolateral akinesia. This study suggested the presence of a left ventricular aneurysm, and led to cardiac catheterization. Coronary arteriography revealed normal coronary arteries. Hemodynamic data were as follows: cardiac output, 5.2 L/min; cardiac index, 2.7 L/min/m^2; pulmonary artery pressure, 26/10 mm Hg; and aortic pressure, 125/75 mm Hg. The levophase of the pulmonary artery injection demonstrated a large apical left ventricular aneurysm with mural thrombus present. A computed tomographic scan of the chest demonstrated a soft tissue mass posterior to the sternum and compressing the heart at the level of the atrioventricular groove.

A period of 6 weeks from the time of original injury was allowed for completion of fibrous maturation of the aneurysm. On October 21, 1980, operation was performed; a midsternal splitting incision was used. A multiloculate hematoma was present in the anterior mediastinum. The medial portion of the right middle lobe of the lung was hemorrhagic and adherent to the hematoma, and therefore was resected. Cardiopulmonary bypass was instituted. The aneurysm was entered, and it was noted that it had not totally matured. Large amounts of mural thrombus were extracted. The endocardium had become fibrous, but the outer portions of the myocardium had not completely fibrosed. Ventricular aneurysmectomy was performed. The ventriculotomy was repaired in three layers over Teflon strips. The patient was weaned from cardiopulmonary bypass without incident. The total time of cardiopulmonary bypass was 53 minutes. Contractility

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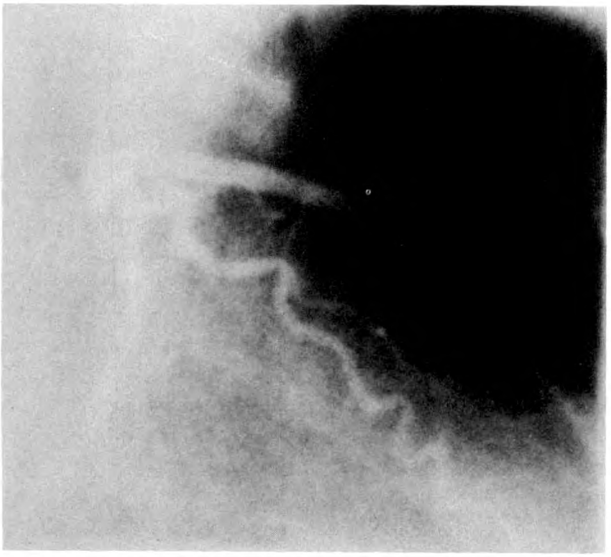

Fig 1. (Patient 2.) Coronary angiogram of the left coronary arterial system (right anterior oblique projection) revealing total occlusion of the proximal left anterior descending coronary artery.

of the left ventricle was good, and systemic pressures were maintained without support.

Postoperatively, the patient recovered without complication. He continues to be a bicycle enthusiast, and remains in New York Heart Association class I.

Patient 2

A 58-year-old woman sustained a deceleration injury to the thorax in an automobile collision. On arrival at a local hospital, the symptoms and clinical findings were suggestive of an acute anterolateral wall myocardial infarction. Approximately 36 hours after admission, acute pulmonary edema developed, and a new systolic murmur was present. The patient was transferred to Loyola University Medical Center.

On arrival the patient appeared tachypneic, restless, and diaphoretic. Blood pressure was 170/110 mm Hg, heart rate was 92 beats per minute and regular, and central venous pressure was 10 mm Hg. Assessment revealed bilateral basilar rales, a left parasternal thrill, and a grade 3/6 high-pitched pansystolic murmur, which was heard best at the left third intercostal space. The ECG showed the presence of first-degree atrioventricular block, and an extensive myocardial infarction of the anterolateral wall (ST elevation noted in leads aVL, I, and V_1 to V_4), left-axis deviation, and left atrial enlargement. A chest roentgenogram revealed bilateral pulmonary congestion. Chemistry analysis revealed prerenal azotemia and the following values: serum glutamic-oxaloacetic transaminase, 2,260; lactate dehydrogenase, 3,010; and creatine phosphokinase, 2,250. Aggressive medical management resulted in clinical improvement.

Cardiac catheterization and coronary angiography by the Sones technique were performed 48 hours after injury and revealed complete occlusion of the proximal LAD before the origin of the first diagonal branch (Fig 1). The circumflex and right coronary artery systems appeared normal. A left ventriculogram in the left anterior oblique position revealed a ventricular septal defect in the superior portion of the ventricular septum. A ventriculogram in the right anterior oblique position showed a large apical aneurysm with paradoxical motion (Fig 2). Hemodynamic data included a left ventricular end-diastolic pressure of 30 mm Hg, pulmonary artery pressure of 40/22 mm Hg, wedge pressure of 29 mm Hg, and 10% oxygen saturation step-up across the tricuspid valve. In light of the recent acute myocardial infarction, medical management was continued.

The patient was readmitted to Loyola University Medical Center 5 months later, and ventricular aneurysmectomy and repair of the ventricular septal defect were performed. At operation, the LAD, which had been totally occluded on the prior angiogram, was patent and fully distended with anterograde flow. No atherosclerotic plaques were palpable along the course of the coronary arteries. The anterolateral portion of the ventricular wall was discolored, fibrotic, and noncontracting, thus representing the location of the previous infarct. Repair of the ventricular septal defect, located at the junction of the anterior wall of the left ventricle and the anterior septum, was performed primarily with pledgeted sutures. The apical aneurysm was resected and closed between Teflon felt strips. The patient was weaned from cardiopulmonary bypass without incident. The postoperative course was uneventful. Fourteen years later the patient remains asymptomatic.

Patient 3

A 20-year-old man was admitted to the emergency room of a local community hospital after sustaining a deceleration injury associated with temporary loss of consciousness during an automobile collision. Because a widened mediastinum was noted on the chest roentgenogram and

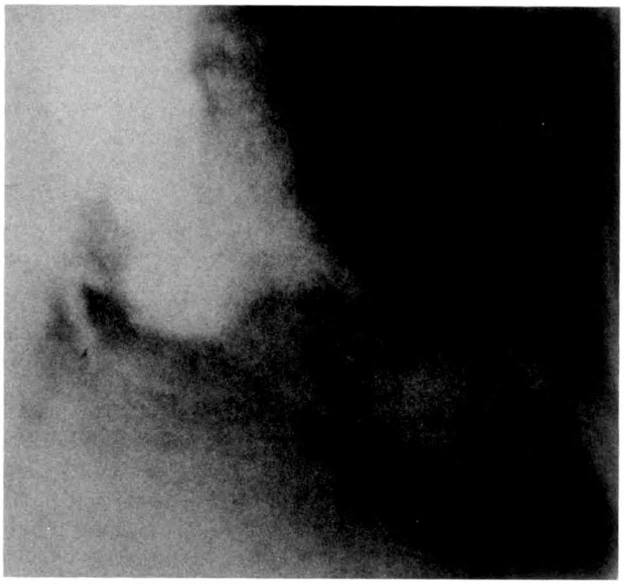

Fig 2. (Patient 2.) Left ventriculogram in systole revealing large apical aneurysm.

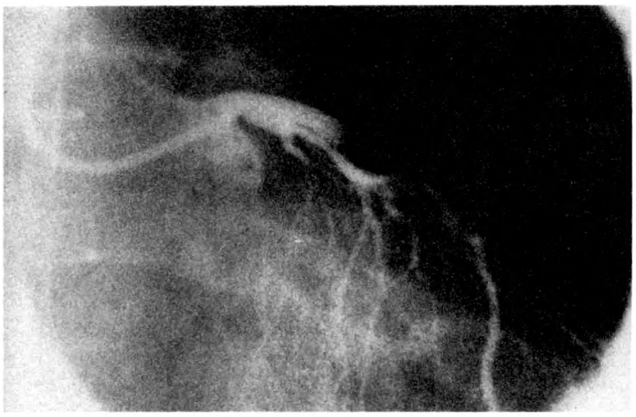

Fig 3. (Patient 3.) Coronary angiogram of the left coronary arterial system revealing total occlusion of the proximal left anterior descending coronary artery.

because the ECG revealed an acute anterolateral myocardial infarction, he was transferred to Loyola University Medical Center.

Physical examination revealed the patient to be awake, alert, and coherent. Blood pressure was 120/68 mm Hg, and heart rate was 104 beats per minute. Peripheral pulses were symmetrically present except for a decreased left carotid pulse. There was no jugular venous distention. The first and second heart rate sounds were normal, and there was no murmur or third heart sound. The neurological examination was normal.

Examination of the chest roentgenogram confirmed a widened mediastinum, and aortography revealed avulsion of the left common carotid artery at its origin from the aortic arch. The ECG revealed an extensive, acute anterolateral myocardial infarction.

The patient was operated on through a midsternal splitting incision, and the heart was examined. A large, clear-cut infarction involving the entire anterolateral wall and apex of the left ventricle was noted. The LAD was collapsed.

The aortic injury was then addressed. It was apparent that an almost complete avulsion of the left common carotid artery had occurred, with the formation of a hematoma at the site of the injury. An 8-mm Dacron graft was anastomosed to the transverse aorta in an end-to-side fashion and to the distal left carotid artery in an end-to-end fashion. The area of the avulsion on the aorta was repaired using Prolene sutures reinforced with strips of Teflon felt.

Postoperatively, the patient's recovery was smooth until the tenth day. At that time, there was evidence of severe left ventricular failure. The possibility of tamponade was considered, but it was thought that an acute ventricular aneurysm was responsible for the heart failure.

An intraaortic balloon was inserted and counterpulsation begun. The patient underwent urgent cardiac catheterization. The coronary arteriogram revealed complete occlusion of the LAD approximately 1 cm from its origin (Fig 3). The circumflex coronary artery arose aberrantly from the right system near the usual takeoff of the conus artery. The other coronary arteries were normal. A large ventricular aneurysm was evident in the anterolateral and apical areas on left ventriculography in diastole (Fig 4A) and systole (Fig 4B).

The patient underwent reoperation to repair the ventricular aneurysm ten days after the first operation. Once cardiopulmonary bypass was instituted, an arteriotomy was made in the LAD proximal to the diagonal branch. A No. 3 Fogarty catheter was then passed proximally, and a large thrombus showing evidence of early organization was extracted. This technique has been previously reported [1]. Once this was done, proximal blood flow was reestablished. Aortocoronary saphenous vein bypass grafting was then performed to the arteriotomy site in the LAD. The left ventricular aneurysm was excised and the

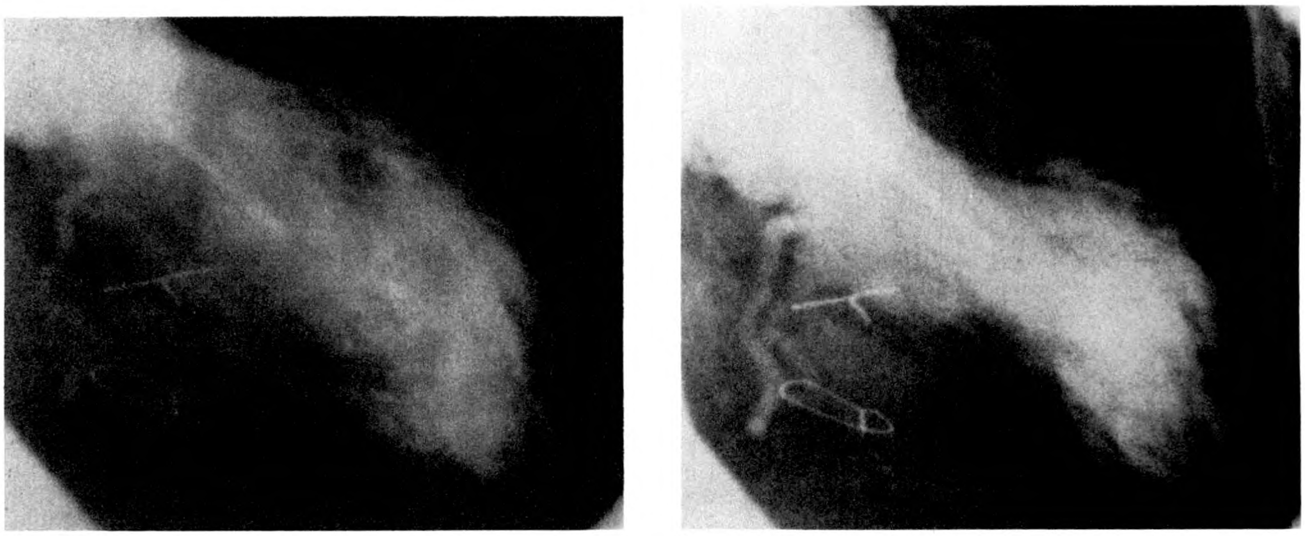

Fig 4. (Patient 3.) Left ventriculogram in (A) diastole and (B) systole revealing a large apical aneurysm.

Table 1. Summary of Data on Patients with Ventricular Aneurysm due to Blunt Chest Injury and Diagnosed at Autopsy

Patient No.	Reference	Year Reported	Age (yr), Sex	Type of Trauma	Manifestation/ Diagnosis	Time to Diagnosis	Complication of Aneurysm	Coronary Anatomy
1	Pontain [2]	1892	40, M	Hit by wagon axle	CHF palpitations	13 mo	CHF	NA
2	Groom [3]	1897	16, M	Thrown from horse	Arrhythmia	1 mo	Rupture	NA
3	French [4]	1912	3, F	Fall	Arrhythmia	20 days	Rupture	NA
4	Fraenkel [5]	1917	20, M	Blast injury	NA	6 mo	CHF	LAD occluded[a]
5	Schminke [6]	1925	45, M	Wagon collision	NA	6 mo	Arrhythmia	LAD occluded[a]
6	Joachim and Mays [7]	1927	12, M	Wagon collision	CHF	13 yr	Arrhythmia	LAD occluded[a]
7	Hawkers [8]	1935	6, M	Motor vehicle accident	Malaise	3 mo	Rupture	NA
8	Hildenbrandt [9]	1938	17, M	Blunt trauma	Arterial embolus	18 yr	Embolus	NA
9	O'Farrell [10]	1938	59, M	Vehicle accident	CHF	3 mo	CHF	NA
10	Pitts and Purvis [11]	1947	10, M	Motor vehicle accident	Weakness		Rupture	NA

[a] This represents an abnormality of the LAD.

CHF = congestive heart failure; LAD = left anterior descending coronary artery; NA = not available.

ventriculotomy closed in three layers using strips of Teflon felt for reinforcement. The patient was weaned from cardiopulmonary bypass without incident, and showed hemodynamic improvement.

Postoperatively, the patient's recovery was uneventful. He is totally asymptomatic 7 years later.

Literature Review

Review of the world literature reveals that 32 cases of left ventricular aneurysm following blunt chest trauma have been reported to date (Tables 1 and 2) [1–30]. This entity was described by Pontain [2] in 1892 when he reported the case of a 40-year-old man who was struck in the chest by a wagon axle. Diagnosis of traumatic left ventricular aneurysm was made at autopsy 13 months later after the development of progressive congestive heart failure.

In 1965, Green and associates [12], at Hammersmith Hospital in London, reported the successful resection of a traumatic left ventricular aneurysm. Previously, the diagnosis of left ventricular aneurysm following blunt trauma had been made at autopsy (see Table 1) after patients had died of the sequelae of untreated ventricular aneurysm, including rupture, congestive heart failure, embolus, and arrhythmia (Table 3).

Our 3 patients bring the total number of patients with left ventricular aneurysm due to blunt chest trauma reported in the literature to 35 (see Tables 1 and 2). Age ranges from 3 to 59 years (median age, 23 years). This group comprises 32 male and 3 female patients. Motor vehicle accidents were the main cause of the blunt injury in these patients. The most common presenting symptoms were congestive heart failure (10 patients), palpitations or arrhythmias (9), and arterial embolus (6). Seven patients had mild constitutional complaints or were asymptomatic. The time from injury to diagnosis ranged from 5 days to 18 years (median time, 3 months). In our 3 patients, the diagnosis was confirmed by cardiac catheterization five, ten, and 18 days after injury.

Prior to the successful resection of a TLVA in 1965, the diagnosis of this condition was made at autopsy. Subsequent to 1965, 23 of 25 patients have undergone successful resection of such an aneurysm. Combined procedures were performed in 3 patients, and included aortocoronary bypass, repair of a ventricular septal defect, and reimplantation of the posterior papillary muscle of the mitral valve. Two patients either refused or were not offered operative intervention.

There were no postoperative deaths (30 days) among those patients undergoing resection of a TLVA. Cerebral emboli occurred in 2 patients at 8 months (fatal) and 1 month (recovered) after operation. Recurrence of a TLVA because of an incomplete resection mandated reoperation in 1 patient. Additional long-term follow-up in this group is not completely available. Our 3 patients are in New York Heart Association class I 6, 15, and 8 years postoperatively.

In 1973, Silver and associates [19] added the 18th patient with left ventricular aneurysm following blunt chest trauma and provided one of the first literature reviews of this topic. They documented total occlusion of the LAD by angiography, and suggested coronary injury as causative in aneurysm formation. In addition, they documented that 5 of 17 patients with a TLVA had occlusion of the LAD. Silver and co-workers suggested that direct coronary artery injury (specifically to the ante-

Table 2. Summary of Data on Patients with Ventricular Aneurysm due to Blunt Chest Injury Since 1964

Patient No.	Reference	Year	Age (yr), Sex	Type of Trauma	Manifestation	Time to Diagnosis	Catheterization	Coronary Anatomy	Surgical Procedure	Outcome
11	Green et al [12]	1965	10, M	Motor vehicle accident	Palpitations	2 mo	Yes	NA	Resection	Survived
12	Cuendet et al [13]	1966	21, M	Blunt	Tachycardia	1 mo	NA	NA	Resection	Survived
13	Waldenhausen et al [14]	1966	5, M	Kicked by horse	NA	15 mo	Yes	NA	Resection	Survived
14	Glancy et al [15]	1967	23, M	Blunt	Arterial embolus	32 mo	Yes	NA	Resection	Survived; cerebral embolus
15	Keller et al [16]	1969	36, M	Motor vehicle accident	NA	2 yr	Yes	NA	Resection	Survived
16	Pupello et al [17]	1970	17, M	Motor vehicle accident	NA	7 days	Yes	NA	Resection	Survived
17	O'Reilly et al [18]	1970	12, F	Fall from bicycle	Murmur	14 mo	NA	NA	Resection	Survived
18	Silver et al [19]	1973	33, M	Motor vehicle accident	CHF	3 mo	Yes	LAD occluded[a]	Resection	Survived
19	Basta et al [20]	1973	43, M	Motor vehicle accident	Arrhythmia	1 yr	Yes	LAD patent	Resection	Survived
20	Doty et al [21]	1974	46, M	Kicked by horse	Palpitation	9 yr	NA	NA	None	Died
21	Doty et al [21]	1974	22, M	Nonpenetrating gunshot wound	Pulsatile chest mass	3 yr	NA	NA	Resection	Survived
22	Doty et al [21]	1974	33, M	Nonpenetrating mortar wound	Arterial embolus	5 yr	NA	NA	Resection	Survived
23	Singh et al [22]	1975	23, M	Chest blow	Arterial embolus	2 mo	Yes	LAD patent	Resection	Survived; cerebral embolus

24	Sakurai et al [23]	1975	43, M	Motor vehicle accident	CHF	11 mo	Yes	LAD patent	Resection	Survived
25	Berkoff et al [24]	1977	24, M	Motor vehicle accident	Murmur	3 mo	Yes	LAD patent	Resection	Survived
26	Hellman and Rufty [25]	1978	25, M	Motor vehicle accident	NA	3 mo	Yes	LAD tapered[a]	Resection	Survived
27	Hertzeanu et al [1]	1976	14, M	Chest	Palpitation	2 mo	Yes	NA	Resection	Survived
28	Lukacs and Lonyai [26]	1978	33, M	Motor vehicle accident	CHF	2 mo	Yes	LAD: proximal stenosis[a]	Resection	Survived
29	Knauf et al [27]	1979	23, M	Blunt	CHF	5 yr	Yes	LAD shortened[a]	Resection	Survived; incomplete excision; reoperation
30	Moran [28]	1980	26, M	Blunt	NA	13 yr	Yes	LAD: 50% stenosis[a]	None	NA
31	Rheuban et al [29]	1981	17, M	Motor vehicle accident	Mitral regurgitation	6 mo	Yes	LAD patent	Resection + reattachment of papillary muscle	Survived
32	Stone and Fleming [30]	1983	17, M	Motor vehicle accident	CHF	5 yr	Yes	LAD: aneurysm[a]	Resection	Survived
33	Grieco et al [present report]	1989	44, M	Bicycle collision	CHF	18 days	Yes	LAD patent	Resection	Survived (5 yr, NYHA class I)
34	Grieco et al [present report]	1989	58, F	Motor vehicle accident	CHF	5 days	Yes	LAD occluded[a]	Resection + VSD repair	Survived (13 yr, NYHA class I)
35	Grieco et al [present report]	1989	20, M	Motor vehicle accident	CHF	14 days	Yes	LAD occluded[a]	Resection + coronary artery bypass	Survived (7 yr, NYHA class I)

[a] This represents an abnormality of the LAD.

CHF = congestive heart failure; LAD = left anterior descending coronary artery; NA = not available; NYHA = New York Heart Association; VSD = ventricular septal defect.

riorly located LAD) with resultant myocardial infarction, rather than localized contusion of the myocardium, was responsible for the development of the ventricular aneurysm.

The pathogenesis of this entity had previously been attributed to "direct myocardial trauma with resulting contusion, hemorrhagic infiltration, necrosis and scar with progressive dilatation of this area forming ventricular aneurysm" [31]. We contend that, rather than localized contusion to the myocardium, an anatomical vascular condition is often present that causes ischemic necrosis and aneurysm formation. The review of the literature was addressed in terms of patency of the LAD (Table 4). Three of the 10 patients diagnosed at autopsy as having a TLVA had occlusion of the LAD. The status of the LAD in the other 7 patients was not mentioned. Twenty-five patients underwent cardiac catheterization, and 8 of the 14 patients in whom the LAD was injected were noted to have the following abnormalities: occlusion (4 patients), stenosis of greater than 50% (3), and aneurysm (1). Six patients had a patent LAD. For 11 patients, no mention of the status of LAD patency was made. Although the small numbers in these groups do not lend themselves to meaningful statistical analysis, this assessment of LAD patency reveals that an LAD abnormality was apparent in at least 11 of the 35 patients in this series.

We contend that the cause of TLVA may be direct injury of the LAD. The likely mechanisms are intimal disruption with thrombosis or intense vasospasm. Angiographic patency of the LAD in some patients might be attributed to recanalization or relief of vasospasm, both of which are poorly quantitable and incompletely understood. Because of the distinct possibility of LAD injury, we support coronary arteriography in patients manifesting electrocardiographic evidence of acute myocardial infarction, cardiogenic shock, or recurrent arrhythmias after blunt chest injury. Ideally, early revascularization might avert the development of a TLVA and its potential complications.

The findings summarized in Table 3 emphasize the lethal nature of complications associated with the presence of untreated ventricular aneurysm. Specifically, 10 of 12 patients who were unable to benefit from surgical resection died of the complications of rupture, embolization, arrhythmia, or congestive heart failure. Review of the literature indicates that resection of left ventricular aneurysms after blunt chest trauma can be performed with minimal morbidity and mortality. Resection should be accepted as the treatment of choice for this clinical entity.

Table 3. Cause of Death Among Patients With Ventricular Aneurysm due to Blunt Chest Injury

Cause	Nonsurgical Group (n = 12)	Surgical Group (n = 23)
Emboli	1	1
Rupture	4	3
Congestive heart failure	3	0
Arrhythmia	2	0
Deaths caused by aneurysm	10/12	1/23

Table 4. Status of the Left Anterior Descending Coronary Artery

Status	No. of Patients
Autopsy findings (n = 10)	
LAD occluded	3
No mention	7
Catheterization findings (n = 20)	
LAD occluded	4
LAD irregular or stenosed	3
LAD with aneurysm	1
LAD patent	6
No mention	11[a]

[a] For 5 of these patients, it is not known whether catheterization was performed.

LAD = left anterior descending coronary artery.

In summary, our experience in managing patients with TLVA and our review of the literature indicate the following:

1. The diagnosis of myocardial contusion encompasses a wide spectrum of myocardial damage produced by nonpenetrating injury. Some patients with this diagnosis have sustained a transmural infarction and are subject to its morbidity and complications.
2. Acute electrocardiographic evidence of myocardial infarction, cardiogenic shock, or recurrent arrhythmias mandates early cardiac catheterization followed by the pertinent treatment.
3. Ventricular aneurysm following blunt chest injury is associated with complications similar to those of aneurysm associated with coronary artery disease, including arrhythmia, rupture, embolization, and congestive heart failure.
4. A high index of suspicion is required to make the diagnosis of TLVA.
5. When TLVA is diagnosed, ventricular aneurysmectomy should be performed to avert lethal complications.
6. Expected results of such an aneurysmectomy are excellent.

Addendum

Personal communication with Dr John Moran gave further information regarding follow-up of the patient with left ventricular aneurysm after blunt chest injury (patient 30). This patient died suddenly while swimming (likely from arrhythmias). He had refused recommended surgical correction of the left ventricular aneurysm.

The authors thank Laura Cizek for her efforts in the preparation of the manuscript.

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CORRESPONDENCE

Left Ventricular Stress During Extracorporeal Membrane Oxygenation

To the Editor:

We have noted with interest the recent observations of Bavaria and colleagues [1] regarding use of roller pump extracorporeal membrane oxygenation (ECMO) to support the ischemic heart. These authors found that roller pump ECMO does not result in effective cardiac support and actually increases wall stress, and presumably oxygen consumption, by increasing afterload. This conclusion also has been reached by Salisbury and co-workers [2] from experimental work and by Spencer and associates [3] from clinical observations. Because roller pump cardiopulmonary bypass systems have been found to actually worsen left ventricular failure by increasing afterload, attention shifted over the past two decades to left heart support [2–4].

Our group has been interested in the use of ECMO to provide circulatory support after a cardiac catastrophe because ECMO can be implemented rapidly without thoracotomy. In the discussion of their paper Bavaria and colleagues [1] suggest that the use of a pulsatile pump for ECMO instead of a roller pump might decrease afterload and thereby improve results with ECMO. In fact, the findings of our recent experiments support this hypothesis.

In one study we found in normal dogs that use of an ECMO system based on a pulsatile pump, as opposed to a roller pump, decreased the tension time index and myocardial oxygen consumption by approximately 50% and improved endocardial/epicardial blood flow distribution and myocardial energy metabolism [5]. In a subsequent study we showed that use of pulsatile ECMO to unload ischemic canine hearts also resulted in a decrease in tension time index of almost 50% [6]. In addition, when combined with reperfusion, unloading the ischemic heart with pulsatile ECMO resulted in significantly greater myocardial salvage than ECMO using a roller pump [6, 7].

Based on these experimental findings and the previously demonstrated clinical deficiencies of roller pump ECMO [3], we agree with the authors that ECMO using a roller pump is not beneficial to the ischemic failing heart. Beyond this, our experimental results [5–7] have demonstrated that an ECMO system that uses diastolic counterpulsation can significantly unload ischemic hearts and thus has great potential as a cardiac assist device.

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Muscle-Sparing Thoracotomy

To the Editor:

I was rather surprised to read the article "Muscle-sparing posterolateral thoracotomy" by Daniel M. Bethencourt and colleagues [1]. The incision used by Bethencourt and colleagues is quite similar to one that I published in 1973 [2]; furthermore, I showed R. Wuerflein (Reference 2 in the article by Bethencourt and colleagues) how to perform this procedure. In France this approach has been used by many teams for many years.

I would like to make two technical points. First, when retracting the lastissimus dorsi, the incision has to be anteriorly but not posteriorly prolonged. Therefore, it is not a posterolateral but a lateral approach. Second, serratus dissection is not necessary as it is possible to go over directly between two digitations.

Michel Noirclerc, MD

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References

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Foreign Body-Induced Hemoptysis

To the Editor:

We read with interest the report by Pattison and colleagues [1] on recurrent hemoptysis in a teenage girl. It brought to mind a similar puzzling case.

A 17-year-old boy was evaluated in February 1986 for recurrent hemoptysis of 3-month duration. A chest roentgenogram showed an ill-defined density in the basilar segments of the right lower lobe; a computed tomography scan confirmed that finding and showed no other abnormalities. Bronchoscopy demonstrated blood streaking from the right lower lobe basal orifices, but washings were negative for blood. Bronchography revealed severe localized bronchiectasis of the posterior basal segment of the right lower lobe. Middle turbinate biopsy showed normal ciliary ultrastructure. Past history revealed treatment for severe bronchitis in August 1978, November 1979, and February 1983, but chest roentgenograms had previously had negative results.

The hemoptysis cleared during antibiotic administration but recurred each time administration was stopped. A posterior basal segmentectomy was performed in June 1986. Examination revealed an extensive pneumonia surrounding a large bronchiectatic sac that contained a firm, barbed foreign body similar to a

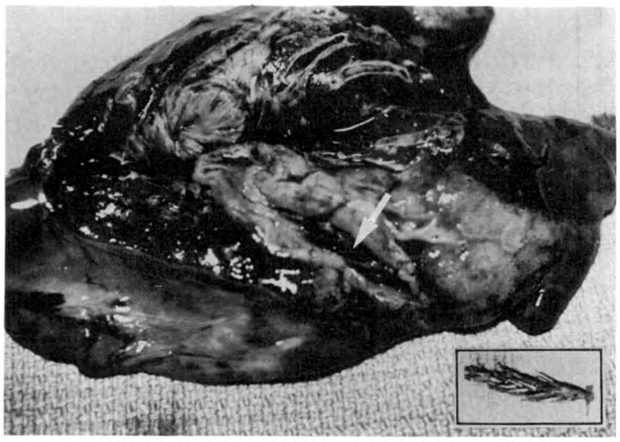

Fig 1. Bronchiectatic sac containing the foreign body (arrow, *inset*), *identified as a seed from a Norfolk Island pine.*

wheat kernel (Fig 1). The patient recovered uneventfully and has had no further hemoptysis.

Upon entering college in September 1986 the patient presented the foreign body to his botany professor, who identified it as a seed from a Norfolk Island pine, a species native to Australia but common in domestic plantings. The patient had no recollection of any episode of aspiration. Clearly, the diagonally oriented seed kernels had acted as barbs, ensuring migration deeper and deeper into the pulmonary parenchyma. It is interesting to speculate whether the earlier episodes of bronchitis were related to this foreign body, although the seed appeared remarkably well preserved.

Robert Lowe, MD
Eric Shore, MD

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Reference

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Right Atrial Cardioplegia: A Safe Procedure for Myocardial Protection

To the Editor:

We read with interest Buckberg's elegant editorial [1] and the fine report from Diehl and colleagues [2] concerning retrograde cardioplegia. Since we described right atrial retrograde cardioplegia (RARC) at the Hospital Broussais in 1983 [3], we have used this technique in more than 3,500 patients: 60% underwent coronary arterial bypass grafting, 30% underwent valvular operations, and 10% underwent miscellaneous other operations. Right atrial cardioplegia was administered at a pressure of 40 to 60 mm Hg. Clamping of the pulmonary artery was undertaken by passing a vessel loop around the aorta and the pulmonary artery through the transverse sinus and pulling this loop to collapse both walls of the pulmonary artery toward the left aspect of the aorta. We believe, therefore, that neither separation of the pulmonary artery from the aorta to gain control of this vessel, as was suggested by Dr Buckberg, nor the use of a large aortic clamp to clamp both aorta and pulmonary artery is necessary [4].

In this series RARC was effective and sufficient in 96% of the cases, whereas in 4% it was necessary to use another method (either cannulation of the coronary artery ostias or antegrade cardioplegia through the aortic root), probably because of the existence of a patent foramen ovale. Moreover, we did not observe in these patients any case of detectable right ventricular dysfunction. Also, regular monitoring of the regional temperatures and perioperative echocardiography [5] showed an excellent distribution of the solution throughout the heart.

On the other hand, although we are aware of and have observed a delay in cardiac arrest when RARC was used, no chemical or hemodynamic disadvantages were noted. Hence, we do not think it is necessary to combine antegrade and retrograde cardioplegia.

We are actually reviewing our experience with RARC in patients operated on for coronary arterial bypass grafting with impared left ventricular function (ejection fraction < 35%). Preliminary results show a slight superiority of this technique over antegrade cardioplegia.

We, like Dr Bonchek, believe that Dr Diehl's very interesting paper provides additional data to prompt each of us to reassess our approach to myocardial protection.

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Victor Jebara, MD
Alain Carpentier, MD, PhD

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75014 Paris, France

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Reply

To the Editor:

Dr Fabiani and colleagues have made a very valuable contribution to myocardial protection in describing and documenting their imaginative technique of right atrial cardioplegia, and their current description of controlling the pulmonary artery will be helpful to those who use their method.

Their enormous experience with this technique reinforces the importance of incorporating retrograde cardioplegia as a mode of cardioplegic delivery for myocardial protection. Right atrial retrograde cardioplegia does, however, require larger volumes to obtain arrest, and also requires multidose administration and warm reperfusion. We have had the clinical suspicion that the large volumes of cardioplegia required may delay temporarily ventricular recovery, and we have recently documented experimentally the potential dangers of high volumes of reperfusion cardioplegia. We have, therefore, tried to limit cardioplegic volume by combining retrograde cardioplegia with antegrade cardioplegia to achieve rapid arrest. Also, we deliver retrograde cardioplegia via the coronary sinus with a catheter that does not require right atrial isolation.

I suspect that Dr Fabiani's review of RARC may indeed show some superiority over antegrade cardioplegia, especially in regard to patients with decreased ejection fraction who cannot undergo complete revascularization and hence cannot have adequate antegrade cardioplegic distribution to contracting areas with poor blood supply. The critical issue, in my view, is how to provide optimum myocardial protection. The answer lies in having experience with both antegrade and retrograde techniques of cardioplegia and combining them to take advantage of their benefits, or using them individually under appropriate conditions.

Gerald D. Buckberg, MD

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Reply

To the Editor:

I appreciate the opportunity to respond to Dr Fabiani and colleagues and to acknowledge the pioneering contributions that they have made in the area of myocardial protection using the retrograde approach. Their method of RARC has greatly simplified the administration of retrograde cardioplegia and will, hopefully, make this approach to myocardial protection more palatable to many cardiac surgeons.

The excellent results described by Dr Fabiani and colleagues in an impressive series of 3,500 patients lend credibility to the effectiveness of RARC. In having applied RARC in several hundred patients undergoing coronary artery bypass operations at the New England Medical Center, we also have not noted any clinically detectable right ventricular dysfunction. Recent work from our laboratory has demonstrated superior preservation of right ventricular function when RARC was compared with antegrade cardioplegia in a canine model of acute right ventricular ischemia and reperfusion [1].

We continue to believe that the administration of an initial dose of antegrade cardioplegia is a useful adjunct to RARC. This initial dose of antegrade cardioplegia is easy to administer and achieves rapid diastolic arrest. This simple addition to the method of Dr Fabiani and colleagues avoids an initial interval after application of the cross-clamp when the heart is ischemic and fibrillating.

We are expanding our use of RARC in patients undergoing coronary artery bypass operations and believe that the technique is safe and well suited for patients with poor preoperative left ventricular function.

James Diehl, MD
Richard J. Cleveland, MD

Department of Surgery
New England Medical Center
750 Washington St
Boston, MA 02111

Reference

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A Simplified Method for Pleural Abrasion

To the Editor:

Abrasion of the parietal pleura as an adjunctive treatment for recurrent pneumothorax and pleural effusions [1] is commonly accomplished by abrading the pleural surface with a dry gauze sponge through a small anterior or transaxillary thoracotomy. We have developed a rapid and easy method that uses the commonly available Bovie tip scraping pads, and have used it successfully in 12 patients. Before beginning the abrasion maneuvers, the surgeon places a second set of gloves on the right and left hands, and the Bovie scraping pad is glued to the volar aspect of the right hand. The pleura is then abraded by scraping motions with the hand inside the wound. Applying another pad to the left hand allows reaching areas that could not be abraded with the right hand. After pleurodesis is completed, the second set of gloves is removed, freeing the hand of the pad without tearing the gloves. This method is quicker and gives a more effective and uniform abrasive result than dry gauze. The Bovie scraping pad maintains the abrasive effect even when it becomes wet, whereas the gauze must be frequently exchanged for a dry one when it becomes too moist. On occasion the most remote areas can be reached, even through extremely small incisions, by mounting the Bovie pad on a ring forceps. We have also mounted portions of the pads on long forceps and performed mechanical pleurodesis via a mediastinoscope in the course of thoracoscopy.

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E. A. Rendina, MD
F. Venuta, MD

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Reference

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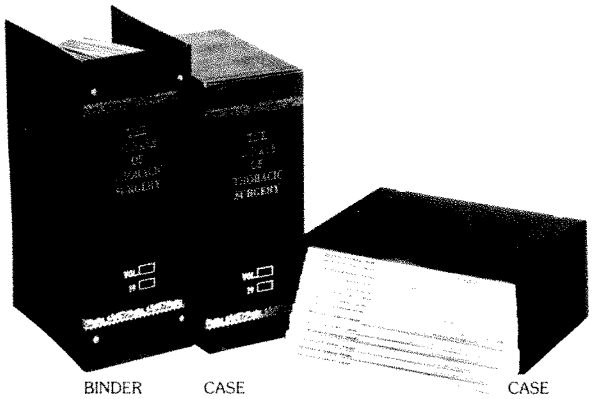

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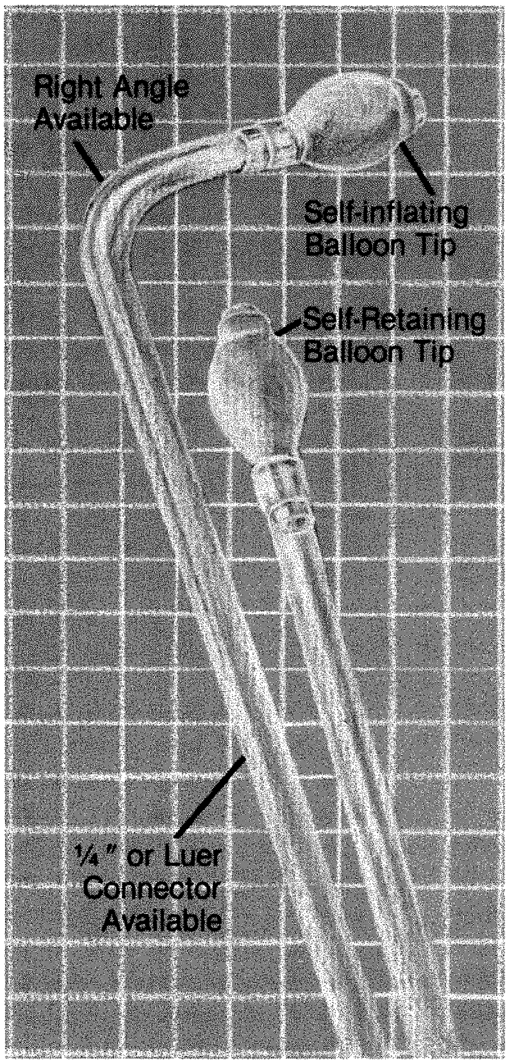
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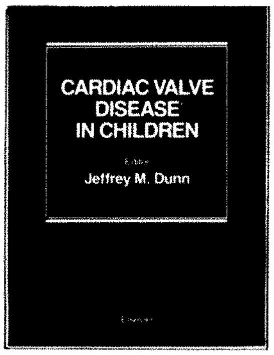

Edited by: **Jeffrey M. Dunn, MD**
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For information on this meeting, contact Omar Prakash, MD, Thorax Centre, Erasmus University, PO Box 1738, 3000 DR Rotterdam, the Netherlands; or telephone 31-10-4635230 (telex: 25267; facsimile: 31-10-4362841).

International Society for Heart Transplantation, Munich, Federal Republic of Germany—April 23–25, 1989

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Sixty-ninth Annual Meeting of The American Association for Thoracic Surgery, Boston, Massachusetts—May 8–10, 1989

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First International Symposium on Heart Failure: Mechanisms and Management, Jerusalem, Israel—May 21–25, 1989

This meeting is sponsored by the Israel Heart Society. For information, contact the Secretariat, First International Symposium on Heart Failure, PO Box 50006, Tel Aviv 61500, Israel; or telephone (03) 654571 (telex: 341171 KENS IL; facsimile; 972-3-655674).

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Twenty-fifth Annual Meeting of The Society of Thoracic Surgeons, Baltimore, Maryland—September 10–13, 1989

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Thirty-eighth Annual Meeting of The Scandanavian Association for Thoracic and Cardiovascular Surgery and The Scandanavian Society for Extracorporeal Technology, Aarhus, Denmark—September 13–16, 1989

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Cardiothoracic surgeon, BE/BC, wanted to join surgeon developing new program scheduled to begin spring 1989 in major southeastern city. Practice will include adult cardiac, thoracic, and peripheral vascular surgery. Will consider experienced individuals or those completing training June 1989. Salary and partnership negotiable. Please send curriculum vitae and recent photograph.

Please respond to A-902, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

2-Man thoracic and cardiovascular surgery group in the Southeast looking for new associate to do thoracic, cardiac, and vascular surgery. Must be board eligible or board certified in thoracic and cardiovascular surgery and have completed training in the recent past or by July 1, 1989.

Please respond to A-910, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiac surgeon sought for beautiful Rocky Mountain region. 200+ cases per year in a 282-bed regional hospital. Excellent salary and benefits with bonus incentives leading to partnership after the third year. Outdoor activities abound in excellent living environment. Board certified/eligible required. Please respond with curriculum vitae and references.

Please respond to A-100, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiovascular and thoracic surgeon, board eligible or certified, wanted to join another surgeon in private practice in the Southeast. Please respond with curriculum vitae.

Please respond to A-101, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Thoracic and cardiovascular surgeon wanted to join a busy practice. Prefer recent graduate. Must be board certified or eligible. Located in Midwest. Please respond with curriculum vitae.

Please respond to A-105, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiothoracic/vascular surgeon: B/C in general and thoracic surgery. Minimum two years of practice experience. Very active private three-surgeon practice. Located in western Pennsylvania. Salary leading to full partnership. Excellent benefits. Detailed CV must accompany response. All replies treated confidentially.

Please respond to A-107, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

The Department of Surgery and Division of Cardiothoracic Surgery has immediate openings for Clinical Fellows in Adult and Pediatric Cardiothoracic Surgery.

Please respond to T. D. Ivey, MD, Division of Cardiothoracic Surgery, Department of Surgery, University Of Cincinnati Medical Center, 231 Bethesda Avenue, Cincinnati, OH 45267-0558.

Cardiothoracic surgeon wanted to join three surgeons in idyllic small city in Eastern Pennsylvania 1.5–2.5 hours drive from major metropolitan centers and Chesapeake Bay. Opportunity to participate in challenging, broadly based practice including electrophysiologic surgery, mitral valve reconstruction, and homograft aortic valve replacement, as well as pulmonary and esophageal surgery. Computerized data base for clinical research. Expanding case load currently over 800 adult open heart and 125 major thoracic procedures annually. Candidate must be current or quite recent trainee of front rank University center with outstanding clinical and technical skills, as this exceptionally busy practice will provide major responsibility immediately, and salary progressing to partnership.

Please respond to Lawrence I. Bonchek, MD, 555 N Duke St, Lancaster, PA 17603; telephone (717) 295-8395.

Cardiothoracic surgeon, BE/BC, wanted to join surgeon in active cardiac/thoracic/vascular surgical practice in northern Alabama community of 80,000 (300,000 population draw). Clinical practice in two community hospitals. Lake/mountain recreation facilities. Generous compensation, future partnership.

Please write: Sara Fleming, Business Manager, 206 Bay St, Gadsden, AL 35901; telephone (205) 543-7501.

Cardiothoracic surgeon, BC/BE, recent graduate, to join 3-man group for private practice in 500-bed teaching hospital, Great Lakes area, currently active in cardiac procedures. Practice includes open heart, thoracic, and vascular and pacemaker cases. Replies kept confidential. Send CV, list of cases, and references.

Please respond to A-108, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiac surgeon needed for active adult practice (450 cases/yr) in New England. Unusual combination of private practice and active research laboratory such that interest in research and academic productivity would be looked at favorably. Need for individual to assume responsibility for patient care immediately and desire to join a close-knit group with salary leading to partnership.

Please respond to A-109, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Pediatric cardiothoracic surgeon: The State University of New York at Buffalo Department of Surgery is seeking applications for an academic pediatric cardiothoracic surgeon to assume a leadership role at one of its major teaching hospitals. The position offers an excellent opportunity for the development of a clinical practice and the initiation of clinical and laboratory investigation. Individuals with major interest and experience in research are preferred and must qualify for a full time faculty appointment in the Department of Surgery. The position includes participation in the departmental graduate and undergraduate teaching program. The State University of New York at Buffalo is an affirmative/equal opportunity employer with a special interest in identifying prospective minority and women candidates.

Applicants should send curriculum vitae to: Robert M. Mentzer, Jr, MD, Department of Surgery, State University of New York at Buffalo, 100 High Street, Buffalo, New York 14203.

Cardiovascular surgeon wanted to join a 2-man group in an established practice in the Southeast. Would prefer a recent graduate, but all applications considered. Generous salary leading to partnership. Practice includes all aspects of adult cardiac, thoracic, and vascular surgery. Send curriculum vitae with experience, recommendations, and photograph.

Please respond to A-110, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiothoracic surgeon needed for rapidly expanding program located in a coastal area of the Southeast. Private practice, primarily adult cardiac and thoracic. BC/BE required. Respond with curriculum vitae, photograph, and names of references.

Please respond to A-111, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Thoracic and vascular surgeon, board certified or board eligible, for very active noncardiac thoracic-vascular practice. Private group in northern New Jersey. Full partnership after acceptable period.

Please respond with curriculum vitae to A-112, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Thoracic and peripheral vascular surgeon needed for busy academically oriented practice in Northern Ohio. Clinical appointment to medical school possible. Only board eligible or board certified surgeons need apply.

Please respond with curriculum vitae to A-113, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiovascular and thoracic surgeon: Position available for a board certified or eligible cardiovascular and thoracic surgeon to join a 3-man private practice involved with adult cardiac, thoracic, and peripheral vascular surgery in a desirable eastern metropolitan area. Association will lead to competitive salary, excellent fringe benefits, and early partnership.

Please respond with curriculum vitae to A-114, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiothoracic surgeon wanted to join a busy practice of cardiac surgery in Connecticut. Please send curriculum vitae outlining surgical experience and training. Recommendations are welcome.

Please respond to A-115, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Assistant Professor of Surgery, cardiothoracic surgery. This is a 3-year appointment with emphasis in clinical congenital heart surgery, laboratory models related to congenital heart disease, and transplantation. Applicants must be board eligible or certified in thoracic surgery and should have had fellowship training in congenital heart surgery. Deadline for receipt of applications is 3/1/89.

Submit complete curriculum vitae to John C. Baldwin, MD, Professor and Chief, Cardiothoracic Surgery, Yale University School of Medicine, 333 Cedar Street, PO Box 3333, New Haven, CT 06510. Yale University is an affirmative action/equal opportunity employer.

Assistant Professor of Surgery, cardiothoracic surgery. This is a 3-year appointment with emphasis in general thoracic surgery, adult cardiac surgery, and experimental laboratory. Applicants must be board eligible or certified in thoracic surgery. Deadline for receipt of applications is 3/1/89.

Submit complete curriculum vitae to John C. Baldwin, MD, Professor and Chief, Cardiothoracic Surgery, Yale University School of Medicine, 333 Cedar Street, PO Box 3333, New Haven, CT 06510. Yale University is an affirmative action/equal opportunity employer.

Faculty position: The Division of Thoracic and Cardiovascular Surgery, Southwestern Medical School of the University of Texas Southwestern Medical Center, is seeking an individual with strong clinical background in adult cardiovascular/thoracic surgery, along with a commitment to education and research, for a position at the assistant professor level. Must be ABTS certified or eligible.

Send complete curriculum vitae to W. Steves Ring, MD, Chairman, Division of Thoracic and Cardiovascular Surgery, UT Southwestern Medical Center, 5323 Harry Hines Boulevard, Dallas, TX 75235-9031. An equal opportunity employer.

Cardiothoracic surgeon wanted to join busy private practice group in excellent northern Florida location.

Please respond to A-116, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiovascular and thoracic surgeon: BE/BC wanted to join progressive, established cardiovascular/thoracic surgeon in a 72-doctor multispecialty group in a Big-10 University community of 100,000 with superb cultural advantages. Initial guarantee and fringes with early associateship. Subsequent income based on productivity.

For confidential consideration, please submit curriculum vitae to A-117, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiovascular thoracic surgeon to join a multisurgeon private practice in the Midwest. Must be board eligible or certified. Must have expertise and experience in all aspects of adult cardiac and thoracic surgery. Generous compensation/future partnership. Send curriculum vitae outlining surgical experience, training, and references.

Please respond to A-118, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Attrition creates need for board certified and experienced cardiovascular/thoracic surgeon to join busy practice of two in Northwest Pennsylvania lakeside location. State-of-the-art facilities and equipment. Research interests can be accommodated. Highly competitive salary and benefit package leads to partnership for appropriate individual.

Please reply to Physician International Search, Inc, 4-TS Vermont St, Buffalo, NY 14213; 1-800-622-4062.

Cardiovascular and thoracic surgeon. Excellent opportunity for a board certified or eligible cardiovascular and thoracic surgeon with experience in surgical interruption of accessory pathways to join a busy Northeastern 5-man group. Practice specializes in adult cardiac and thoracic surgery. Excellent benefit package.

Please reply with curriculum vitae to Cardio-Thoracic Associates of Western New York, PC, 1275 Delaware Avenue, Buffalo, NY 14209.

Unexpected vacancy in approved thoracic and cardiovascular residency training program beginning July 1989. Applicant must be board eligible/certified in general surgery.

Please respond to A-119, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

General, thoracic, and vascular surgeon (no open heart): Two general and one vascular surgeon need a thoracic, vascular, and general surgeon to round out a very busy practice on Long Island. Superb opportunity leading to partnership.

Please respond to A-120, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

SITUATIONS WANTED

Cardiovascular and thoracic surgeon, 34, recent graduate, ABS certified, ABTS eligible. Additional year of experience in all aspects of cardiac surgery. Wishes to join an active cardiothoracic practice. Curriculum vitae, operative experience, and references available upon request.

Please respond to W-545, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiothoracic surgeon, 38, ABS, ABTS, university trained with academic and private practice experience, wishes to relocate, preferably in the New England area. Strong patient care skills, experienced in internal mammary artery grafting, redo operations, and left ventricular assist device. Curriculum vitae and references available upon request.

Please respond to W-550, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Pediatric cardiac surgeon, university-trained with additional fellowship training in congenital heart surgery; seeking an academic position in cardiothoracic surgery with primary responsibility to infants and children. Experience with research and publication and interested in investigating neonatal myocardial ischemia, protection, and preservation; available July 1989.

Please respond to W-548, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiovascular and thoracic surgeon, 42, American, ABS, ABTS, ABVS. Eight years private practice experience. Completing overseas fellowship in heart and heart/lung transplantation July 1989. Seeks opportunity with program involved in transplant surgery. Curriculum vitae and references upon request.

Please respond to W-546, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiovascular and thoracic surgeon, mid-50's. University trained, ABS/ABTS, 14 years of extensive and highly successful solo practice in vein and IMA CABG, valve, pulmonary and vascular surgery. Experienced in starting open heart program. Strong surgical and clinical skills. Seeking private practice opportunity, either starting new program or in association with established individual or group.

Please respond to W-100, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiovascular and thoracic surgeon, 40, wishes to relocate, preferably in the Southeast. American university trained, ABS, ABTS, FACS. Private practice experience in adult cardiac, thoracic, and peripheral vascular surgery. Willing to initiate new program. Curriculum vitae and references upon request.

Please respond to W-101, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Pediatric and adult cardiothoracic surgeon, 33, board eligible, available July 1989. Extensive training in superior Northeastern cardiothoracic surgical program. Experienced in adult coronary and valvular surgery, pediatric cardiac surgery, reoperations, internal mammary artery surgery, aortic surgery, and heart transplantation. Curriculum vitae and references upon request.

Please respond to W-102, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiac, vascular, and thoracic surgeon, 50, wishes to relocate. Academic background with numerous publications. Greater than 10 years private practice—set up open heart unit. CV on request.

Please respond to W-103, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiovascular and thoracic surgeon. 31 yr. ABS/BC. Will finish U Toronto CVT residency (ABTS/BE) July 1989. Excellent references. Seek stable private practice association with senior partner(s) in adult cardiac.

40 Baywood Ct. Thornhill, Ontario L3T 5W3 Canada; 416-889-4078.

Cardiothoracic surgeon, 33, ABS certified, ABTS eligible, available July 1989. University trained with experience in IMA grafts, coronary surgery, valvular surgery. Solid exposure to complex congenital surgery and electrophysiology. Seeks private practice situation but would be delighted to accept some academic responsibilities. Prefer Mid-to-North Atlantic states or Midwest.

Please respond to W-104, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Chief resident in cardiothoracic surgery in major New York training program, finishing June 1989. Interested in private practice in Northeast. Curriculum vitae and references upon request.

Please respond to W-105, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

FELLOWSHIPS

Fellowship in thoracic and cardiovascular surgery available July 1989.

Contact Dr Harold C. Urschel, 3600 Gaston Avenue, Suite 1201, Dallas, TX 75246; telephone (214) 824-2503.

Fellowship in cardiovascular surgery for 1 year available January 1 or July 1 with group doing approximately 1,000 cardiac procedures per year and large volume of vascular procedures. ABS eligible or certified, California medical license required or readily obtainable. Ideal for a person between general surgery residency and thoracic surgery residency.

Please respond with curriculum vitae to Bradley J. Harlan, MD, 5301 F Street, Suite #312, Sacramento, California 95819.

Surgical fellow: Clinical fellowship position available in adult and pediatric cardiothoracic surgery. Large volume of cases. NJ license required. Excellent salary and benefits.

Please contact Lorenzo Gonzalez-Lavin, MD, Dept of Surgery, Deborah Heart & Lung Center, Browns Mills, NJ 08015.

Research fellowship in thoracic oncology available for 2 to 3 years. Projects include the immunology and biology of lung cancer and studies on mechanisms of metastases. Salary is supported by an NIH Training Grant.

Send curriculum vitae and three references to Dr Jack A. Roth, Chairman, Department of Thoracic Surgery, Box 109, University of Texas MD Anderson Hospital and Tumor Institute, 1515 Holcombe Blvd, Houston, TX 77030. An equal opportunity/affirmative action employer.

Clinical fellowship in adult cardiothoracic surgery available. Excellent stipend and fringe benefits.

Please send curriculum vitae to Eldred D. Mundth, MD, Bryn Mawr Medical Building, North, 830 Old Lancaster Road, Bryn Mawr, PA 19010.

Cardiac surgery research fellowship: Research fellowship in cardiac surgery available for 1–2 years beginning in July 1989. Major projects include laboratory and clinical research in cardiomyoplasty, the use of skeletal muscle for cardiac assist. Position also provides access to leading thoracic surgery training program. Salary is negotiable.

Contact James D. Sink, MD, The Emory Clinic, Section of Cardio-thoracic Surgery, 1365 Clifton Road, NE, Atlanta, GA 30333; (404) 321-0111, Extension 3616.

Fellowship, thoracic surgical oncology: Position available July 1989 in the Department of Thoracic Surgery and Oncology at Roswell Park Memorial Institute, Buffalo, NY. Training will focus on diagnosis, treatment, and research in the intrathoracic malignancies, especially lung cancer. Areas of interest include surgery, chemotherapy, immunology, and immunotherapy. Applicants must have had at least 3 years of approved residency training in the US.

Interested candidates should contact H. Takita, MD, DSc, FACS, Chief, Department of Thoracic Surgery and Oncology, Roswell Park Memorial Institute, Elm and Carlton Streets, Buffalo, NY 14263; (716) 845-8574 or 845-2300. An equal opportunity/affirmative action employer.

Cardiopulmonary transplant fellowship. Available July 1, 1989, to June 30, 1990. Active transplant program requires surgeon to assist in donor procurement, operations, and preoperative and postoperative management of patients, as well as recipient evaluation. Position is appropriate for PGY III or higher or for surgeon who has completed thoracic surgery. Deadline for receipt of applications is 3/1/89.

Submit complete curriculum vitae to John C. Baldwin, MD, Professor and Chief, Cardiothoracic Surgery, Yale University School of Medicine, 333 Cedar Street, PO Box 3333, New Haven, CT 06510. Yale University is an affirmative action/equal opportunity employer.

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Resumes and references should be forwarded to Coordinator, Medical Staff Affairs, St. Francis Hospital, 100 Port Washington Boulevard, Roslyn, NY 11576. An equal opportunity employer.

Fellowship in cardiovascular surgery: Clinical training position in adult cardiovascular surgery with emphasis on use of the operating microscope for coronary bypass surgery available July 1989. Generous stipend and fringe benefits.

Please send curriculum vitae with requirements to John Bell-Thomson, MD, Chairman, Division of Cardiothoracic Surgery, Albert Einstein Medical Center, York & Tabor Roads, Philadelphia, PA 19141.

Fellowship in cardiothoracic surgery for 1 year available July 1 in a university-affiliated program. Candidate must be ABS eligible or certified; Pennsylvania medical license required. Excellent salary and all expenses paid including malpractice insurance. Candidate *will be performing* all aspects of adult cardiothoracic and vascular surgery. Opportunities for research and teaching are available. This program is designed for the surgeon who is between a general surgery residency and a thoracic surgery residency.

Please respond with curriculum vitae to Arthur J. Roberts, MD, Director, The Heart Institute, Suite 340, 35 West Linden Street, Wilkes-Barre, PA 18702.

Fellowship in thoracic and cardiovascular surgery available beginning July 1989. Training includes large variety of adult cardiac, general thoracic, pulmonary, and esophageal surgery. Excellent stipend and fringe benefits.

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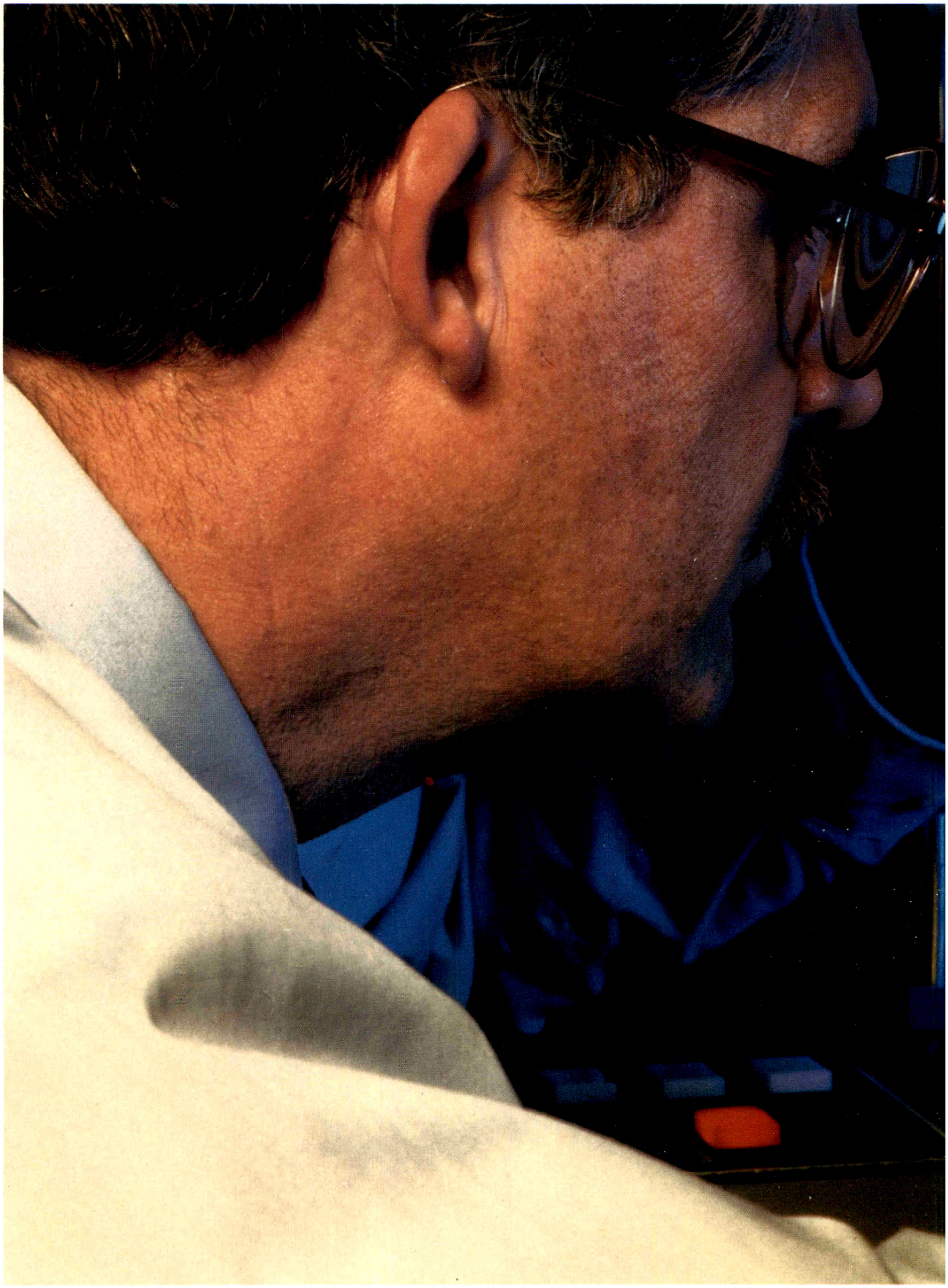

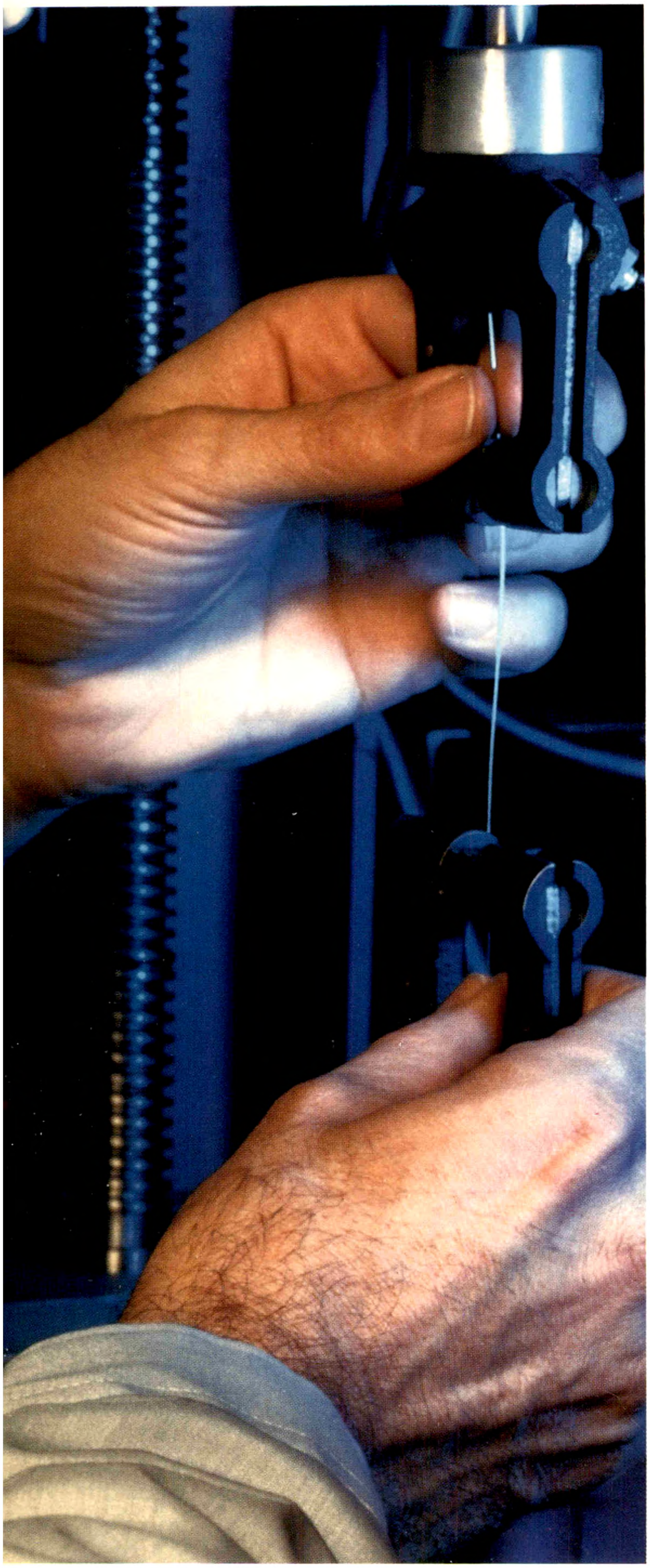

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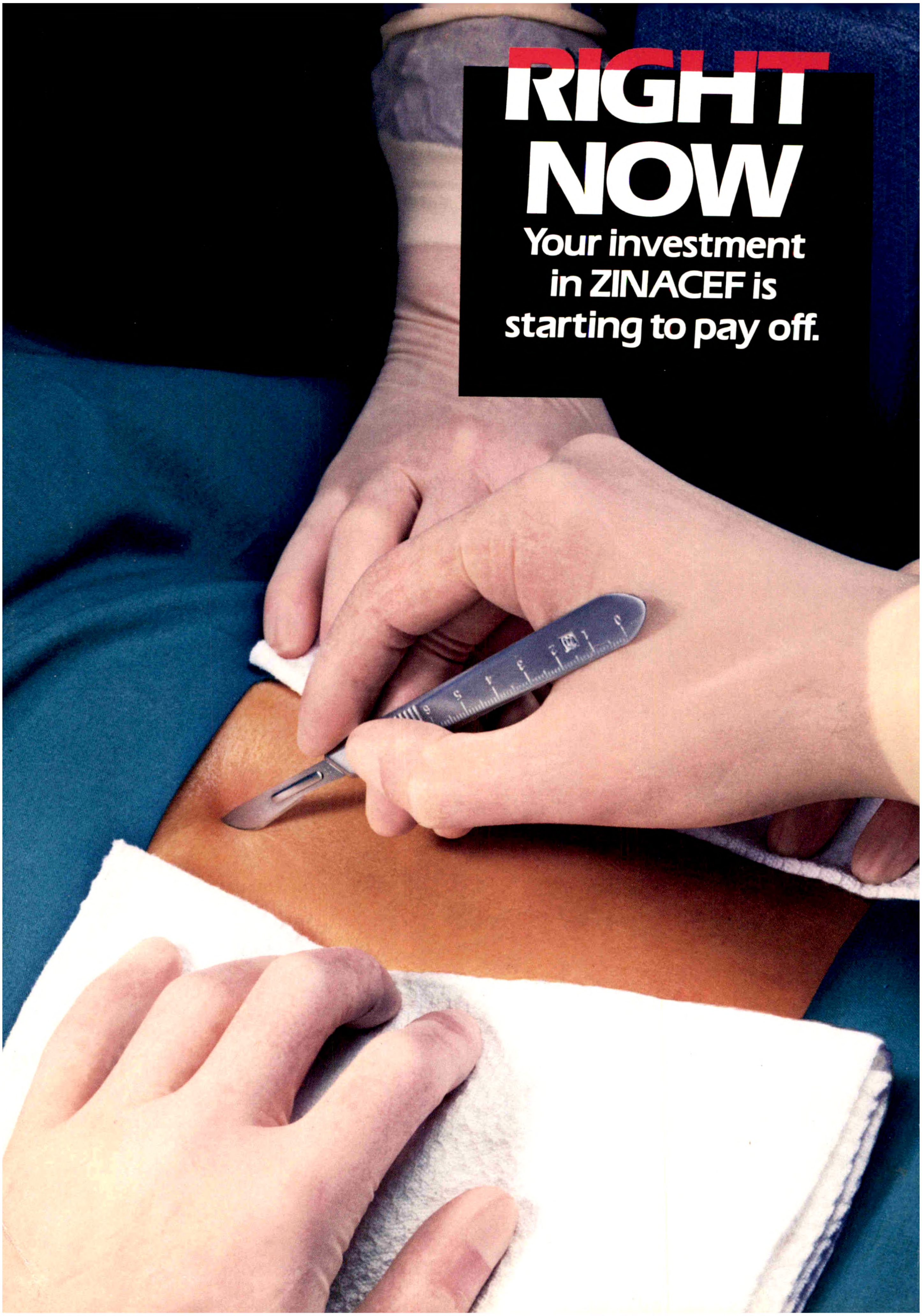
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A recent nationwide analysis revealed that each postoperative wound infection represents a nonreimbursable loss to a hospital of $2,467, on average.[2] By reducing the rate of infection, ZINACEF can help reduce these losses.

1. Slama TG, Sklar SJ, Misinski J, et al: Randomized comparison of cefamandole, cefazolin, and cefuroxime prophylaxis in open-heart surgery. *Antimicrob Agents Chemother* 1986;29:744-747.
2. Haley RW, White JW, Culver DH, et al: The financial incentive for hospitals to prevent nosocomial infections under the prospective payment system. *JAMA* 1987;257:1611-1614.

Please consult Brief Summary of Prescribing Information on next page before prescribing or administering ZINACEF.

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Brief summary. Before prescribing, consult complete Prescribing Information.

INDICATIONS AND USAGE: ZINACEF® is indicated for the treatment of patients with infections caused by susceptible strains of the designated organisms in the following diseases:

1. **Lower Respiratory Tract Infections**, including pneumonia, caused by *S pneumoniae* (formerly *D pneumoniae*), *H influenzae* (including ampicillin-resistant strains), *Klebsiella* sp, *S aureus* (penicillinase- and non-penicillinase-producing), *S pyogenes*, and *E coli*.
2. **Urinary Tract Infections** caused by *E coli* and *Klebsiella* sp.
3. **Skin and Skin Structure Infections** caused by *S aureus* (penicillinase- and non-penicillinase-producing), *S pyogenes*, *E coli*, *Klebsiella* sp, and *Enterobacter* sp.
4. **Septicemia** caused by *S aureus* (penicillinase- and non-penicillinase-producing), *S pneumoniae*, *E coli*, *H influenzae* (including ampicillin-resistant strains), and *Klebsiella* sp.
5. **Meningitis** caused by *S pneumoniae*, *H influenzae* (including ampicillin-resistant strains), *N meningitidis*, and *S aureus* (penicillinase- and non-penicillinase-producing).
6. **Gonorrhea:** Uncomplicated and disseminated gonococcal infections due to *N gonorrhoeae* (penicillinase- and non-penicillinase-producing strains) in both males and females.
7. **Bone and Joint Infections** caused by *S aureus* (including penicillinase- and non-penicillinase-producing strains).

Clinical microbiological studies in skin and skin structure infections frequently reveal the growth of susceptible strains of both aerobic and anaerobic organisms. ZINACEF has been used successfully in these mixed infections in which several organisms have been isolated. Appropriate cultures and susceptibility studies should be performed to determine the susceptibility of the causative organisms to ZINACEF.

Therapy may be started while awaiting the results of these studies; however, once these results become available, the antibiotic treatment should be adjusted accordingly. In certain cases of confirmed or suspected gram-positive or gram-negative sepsis or in patients with other serious infections in which the causative organism has not been identified, ZINACEF may be used concomitantly with an aminoglycoside (see **PRECAUTIONS**). The recommended doses of both antibiotics may be given depending on the severity of the infection and the patient's condition.

Prevention: The preoperative prophylactic administration of ZINACEF may prevent the growth of susceptible disease-causing bacteria and thereby may reduce the incidence of certain postoperative infections in patients undergoing surgical procedures (eg, vaginal hysterectomy) that are classified as clean-contaminated or potentially contaminated procedures. Effective prophylactic use of antibiotics in surgery depends on the time of administration. ZINACEF® (sterile cefuroxime sodium, Glaxo) should usually be given one-half to one hour before the operation to allow sufficient time to achieve effective antibiotic concentrations in the wound tissues during the procedure. The dose should be repeated intraoperatively if the surgical procedure is lengthy.

Prophylactic administration is usually not required after the surgical procedure ends and should be stopped within 24 hours. In the majority of surgical procedures, continuing prophylactic administration of any antibiotic does not reduce the incidence of subsequent infections but will increase the possibility of adverse reactions and the development of bacterial resistance.

The perioperative use of ZINACEF has also been effective during open heart surgery for surgical patients in whom infections at the operative site would present a serious risk. For these patients it is recommended that ZINACEF therapy be continued for at least 48 hours after the surgical procedure ends. If an infection is present, specimens for culture should be obtained for the identification of the causative organism and appropriate antimicrobial therapy should be instituted.

CONTRAINDICATIONS: ZINACEF® is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

WARNINGS: BEFORE THERAPY WITH ZINACEF® IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEPHALOSPORINS, PENICILLINS, OR OTHER DRUGS. THIS PRODUCT SHOULD BE GIVEN CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS. ANTIBIOTICS SHOULD BE ADMINISTERED WITH CAUTION TO ANY PATIENT WHO HAS DEMONSTRATED SOME FORM OF ALLERGY, PARTICULARLY TO DRUGS. IF AN ALLERGIC REACTION TO ZINACEF OCCURS, DISCONTINUE THE DRUG. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE EPINEPHRINE AND OTHER EMERGENCY MEASURES.

Pseudomembranous colitis has been reported with the use of cephalosporins (and other broad-spectrum antibiotics); therefore, it is important to consider its diagnosis in patients who develop diarrhea in association with antibiotic use.

Treatment with broad-spectrum antibiotics alters normal flora of the colon and may permit overgrowth of clostridia. Studies indicate a toxin produced by *C difficile* is one primary cause of antibiotic-associated colitis. Cholestyramine and colestipol resins have been shown to bind the toxin in vitro.

Mild cases of colitis may respond to drug discontinuance alone. Moderate to severe cases should be managed with fluid, electrolyte, and protein supplementation as indicated.

When the colitis is not relieved by drug discontinuance or when it is severe, oral vancomycin is the treatment of choice for antibiotic-associated pseudomembranous colitis produced by *C difficile*. Other causes of colitis should also be considered.

PRECAUTIONS: Although ZINACEF® rarely produces alterations in kidney function, evaluation of renal status during therapy is recommended, especially in seriously ill patients receiving the maximum doses. Cephalosporins should be given with caution to patients receiving concurrent treatment with potent diuretics as these regimens are suspected of adversely affecting renal function.

The total daily dose of ZINACEF should be reduced in patients with transient or persistent renal insufficiency because high and prolonged serum antibiotic concentrations can occur in such individuals from usual doses.

As with other antibiotics, prolonged use of ZINACEF may result in overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

Nephrotoxicity has been reported following concomitant administration of aminoglycoside antibiotics and cephalosporins.

Interference with Laboratory Tests: A false-positive reaction for glucose in the urine may occur with copper reduction tests (Benedict's or Fehling's solution or with Clinitest® tablets), but not with enzyme-based tests for glycosuria (eg, Tes-Tape®). As a false-negative result may occur in the ferricyanide test, it is recommended that either the glucose oxidase or hexokinase method be used to determine blood plasma glucose levels in patients receiving ZINACEF.

Cefuroxime does not interfere with the assay of serum and urine creatinine by the alkaline picrate method.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Although no long-term studies in animals have been performed to evaluate carcinogenic potential, no mutagenic potential of cefuroxime was found in standard laboratory tests.

Reproductive studies revealed no impairment of fertility in animals.

Pregnancy: *Teratogenic Effects: Pregnancy Category B:* Reproduction studies have been performed in mice and rabbits at doses up to 60 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to cefuroxime. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: Since ZINACEF is excreted in human milk, caution should be exercised when ZINACEF is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in children below 3 months of age have not been established. Accumulation of other members of the cephalosporin class in newborn infants (with resulting prolongation of drug half-life) has been reported.

ADVERSE REACTIONS: ZINACEF® is generally well tolerated. The most common adverse effects have been local reactions following intravenous administration. Other adverse reactions have been encountered only rarely.

Local Reactions: Thrombophlebitis has occurred with intravenous administration in 1 in 60 patients.

Gastrointestinal: Gastrointestinal symptoms occurred in 1 in 150 patients and included diarrhea (1 in 220 patients) and nausea (1 in 440 patients). Symptoms of pseudomembranous colitis can appear during or after antibiotic treatment.

Hypersensitivity Reactions: Hypersensitivity reactions have been reported in less than 1% of the patients treated with ZINACEF and include rash (1 in 125). Pruritus, urticaria, and positive Coombs' test each occurred in less than 1 in 250 patients, and, as with other cephalosporins, rare cases of anaphylaxis, erythema multiforme, and Stevens-Johnson syndrome have occurred.

Blood: A decrease in hemoglobin and hematocrit has been observed in 1 in 10 patients and transient eosinophilia in 1 in 14 patients. Less common reactions seen were transient neutropenia (less than 1 in 100 patients) and leukopenia (1 in 750 patients). A similar pattern and incidence was seen with other cephalosporins used in controlled studies.

Hepatic: Transient rise in SGOT and SGPT (1 in 25 patients), alkaline phosphatase (1 in 50 patients), LDH (1 in 75 patients), and bilirubin (1 in 500 patients) levels has been noted.

Kidney: Elevations in serum creatinine and/or blood urea nitrogen and a decreased creatinine clearance have been observed, but their relationship to cefuroxime is unknown.

HOW SUPPLIED ZINACEF® is a dry, white to off-white powder supplied in vials and infusion packs.

Each vial contains cefuroxime sodium equivalent to 750 mg, 1.5 g, or 7.5 g of cefuroxime. ZINACEF in the dry state should be stored between 15° to 30°C (59° to 86°F), and protected from light.

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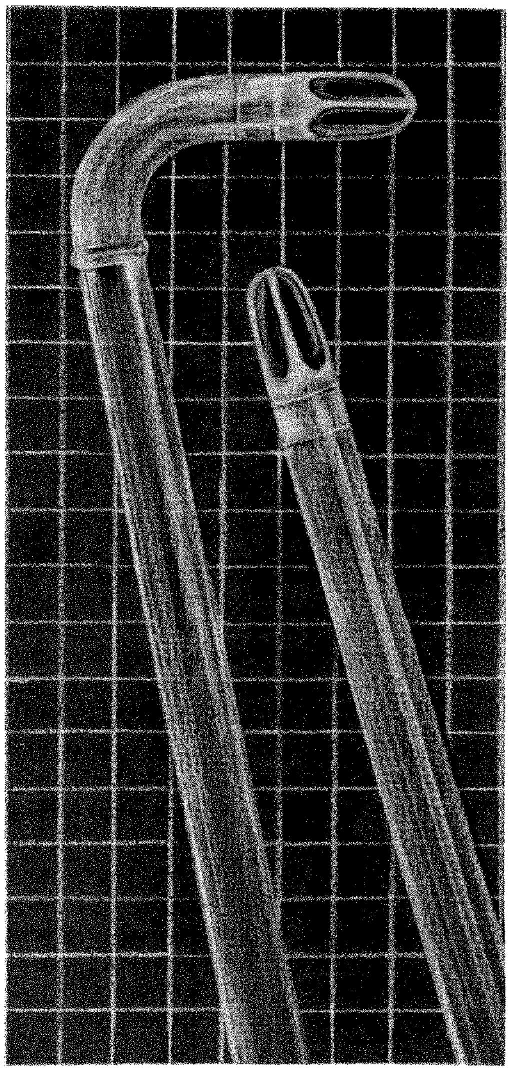

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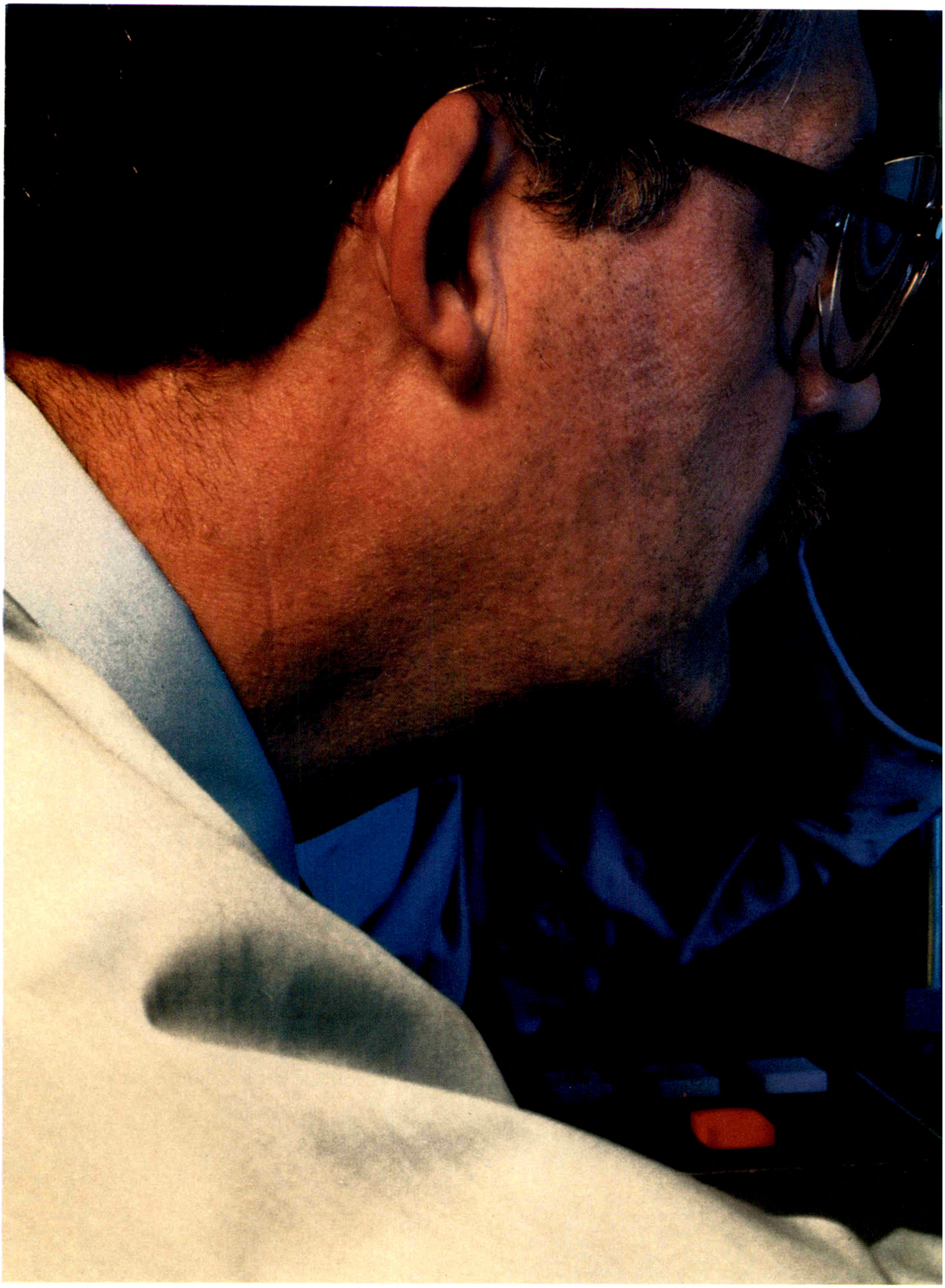

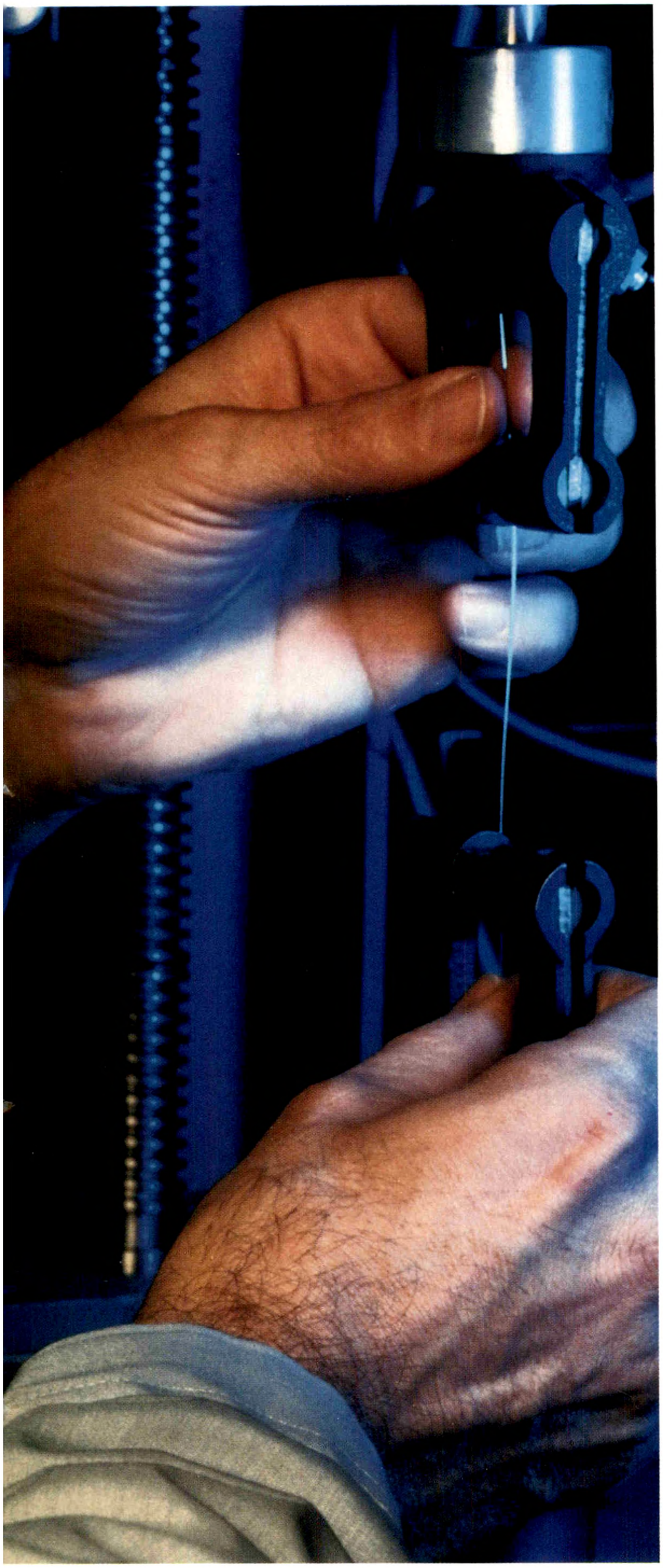

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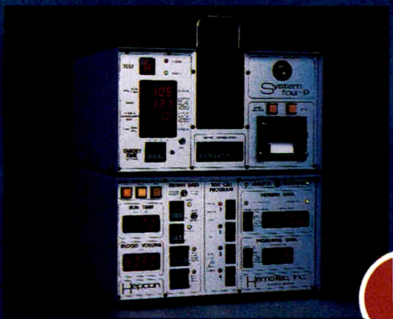

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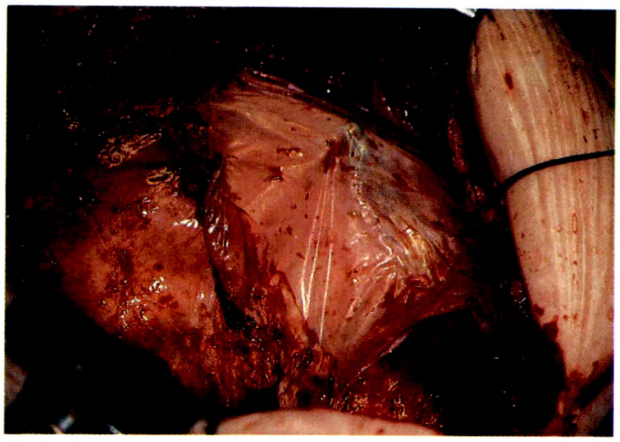

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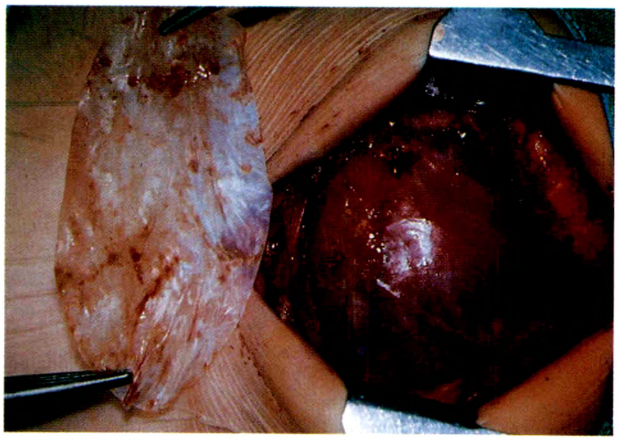

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Choosing Cardiothoracic Surgical Residents

Hermes C. Grillo, MD, and Benson R. Wilcox, MD

General Thoracic Surgery, Massachusetts General Hospital, Boston, Massachusetts, and Division of Cardiothoracic Surgery, The University of North Carolina, Chapel Hill, North Carolina

Most directors of cardiothoracic surgical training programs accept extramural candidates as well those from their own hospitals' general surgical programs. The selection process has been a chaotic one historically. In the competitive effort to get the best people, positions have been offered earlier and earlier in the general surgical resident's career. Although the general caliber of such candidates has been good, there have been numerous instances of premature selection in which candidates proved to be ill adapted to cardiothoracic surgery by the time they commenced a program. Sometimes selection has been based on the reputation of the institution at which the resident was taking his or her general surgical training; by the time that institution had learned the worst about the candidate, he or she was already slated for a cardiothoracic program. For the residents themselves, this early selection process posed enormous problems. They were unable truly to select their most preferred programs. The surgical resident who decided later to enter cardiothoracic surgery found that many preferred programs were already closed by prior selection.

In an effort to introduce order and fairness to the process, a matching program in cardiothoracic surgical residencies was commenced in 1987 under the auspices of the National Residency Matching Program (NRMP). Under this program the participating institutions agreed to accept applicants at specified dates and to make decisions about their choices in numerical order by a fixed date approximately 2 years before commencing residency. Although it is acceptable for a program director to indicate his interest in a candidate, the agreed upon rules are that the final selection will be made through the NRMP and that no commitment will be extracted from the applicant. On the part of the applicants, the requirements are that they list their choices in numerical order and do not make prior commitments to any program in the match even if such a program irregularly and unethically requests such a commitment.

It is clear that if all programs, except those that select their residents only from their own institution's general surgical program and an occasional specially constructed program that is interwoven with general surgery, were to participate in this plan and follow the rules, orderliness and fairness would enter the selection process. The advantages to the trainee would be to reduce confusion and anxiety and remove the pressures to make a premature choice where he or she would prefer to have a battery of choices at an appropriate time. The program directors would lose absolutely nothing by such a system. The most competitive programs would still continue to get excellent candidates. It would avoid the hazards of premature selection before the individual had developed far enough in his or her interests and performance and it would give to the whole process an orderly progression.

The match has been accepted with some hesitation and suspicion. Change is always difficult, particularly for the conservative surgical nature. One would think that there would be enough historical memory of the totally frenetic and chaotic selection process in general surgical residencies that preceeded the present matching programs to convince directors to give the NRMP in thoracic surgery a chance. Unfortunately, a number of strong programs have elected not to participate or have withdrawn from participation fearing that they might lose a chance to recruit good candidates who might be prematurely selected by other strong programs. Also, unfortunately, even within the structure of the NRMP, a number of programs have not played according to the agreed upon rules. Thus, there was even an instance in which a candidate was asked to sign a contract before the NRMP matching.

It seems that it is time to stand back and think for a moment about what our goals and objectives are in constructing and directing cardiothoracic surgical training programs. The motivations are obvious and are several. These include the desire to instruct and transmit knowledge, a venerated and respected tradition in surgery. Most of us are also convinced that a well-run training program provides superior care for our patients. Less tangible is the stimulation from interchange with young surgeons in training, which extends from standard surgery to innovative approaches and laboratory experimentation. Prestige and pride must also be recognized, even if with less approval.

Less laudable are motivations that include the acquisition of additional hands to accomplish the day's tasks, at levels that the physician assistant cannot provide, and the protection from personal demands on the surgeon that a good resident can and does provide.

If we think as educators, we believe that we would all conclude that a well organized, universally applicable, and ethically conducted matching program would provide the best system from the trainees' point of view. It would also lead to no decline in the strength of the residents available to individual programs, although there would be an occasional adjustment in the specific individuals selected for a program. There are times when collegial activity is necessary in our profession to accomplish desirable goals. Perhaps we should ask ourselves whether we are educators or entrepreneurs. We believe it is time to forego a little selfishness for desirable common goals. It seems especially to be the obligation of outstanding educational programs to take the lead in making the matching program a success.

Address reprint requests to Dr Grillo, Massachusetts General Hospital, 32 Fruit St, Boston, MA 02114.

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Esophagectomy for Achalasia: Who, When, and How Much?

F. Henry Ellis, Jr, MD, PhD

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In this issue, Orringer and Stirling [1] propose a bold approach to the surgical management of certain cases of esophageal achalasia, namely, transhiatal esophagectomy with cervical esophagogastrostomy. It is an approach with which I agree in part. Our results with less radical reoperative procedures on the achalasic esophagus were suboptimal and led my colleagues and myself [2] to suggest that consideration be given to a radical operative procedure, although the precise indications for such an approach were not clear at the time. We later suggested [3] that this procedure be reserved for patients who had previously undergone multiple esophageal operations or who had megaesophagus after one myotomy had failed. The indications for resection proposed by Orringer and Stirling are more liberal than ours, and their operation is more radical.

The approach they are suggesting is not new. The South Americans have had considerable experience with esophagectomy when treating patients with advanced megaesophagus (greater than 7 cm in diameter) secondary to Chagas' disease [4]. Orringer and Stirling define megaesophagus as an esophagus with a diameter of 8 cm or more. This definition is comparable with what we have classified as a severe form of the disease. Our results after esophagomyotomy in such instances have been similar to those in patients with a less advanced form of the disease. Four patients with megaesophagus reported on by Orringer and Stirling were treated primarily by resection without a previous myotomy, an approach with which I am in disagreement in view of our experience.

If megaesophagus is defined as a sigmoid-shaped saclike structure that is huge and dilated, then esophagomyotomy, even when properly performed, may not be accompanied by adequate emptying of the enlarged organ. Whether total resection as the primary procedure is warranted or not has yet to be determined. My associates and I have treated a few such patients by segmental esophagectomy to shorten the organ, coupled with elliptical excision of the lateral wall of the esophagus at the time of esophagomyotomy to narrow it, with surprisingly good results. Others [5] have recommended esophagoplication when myotomy is performed to eliminate the sigmoid-shaped sac that interferes with proper emptying. Further experience with these more limited approaches to the management of megaesophagus is worth pursuing, although total esophagectomy has the theoretical appeal of removing the entire diseased esophagus and rids the patient of the slight but definite risk of malignant degeneration. Even after a successful myotomy, a carcinoma may develop in the achalasic esophagus many years later [6].

After a failed myotomy, and in the absence of megaesophagus, when should total esophagectomy be resorted to? It is not clear to me whether Orringer and Stirling propose the performance of this procedure in every patient who has failed to respond to an esophagomyotomy or whether the patients who are the subject of their paper represent a selected group in whom myotomy has failed. I suspect their current belief is that all patients who fail to improve after an esophageal operation for achalasia should have an esophagectomy. If this approach is adopted, one has to recognize the risks involved, which are not insignificant. In this small series, complications included postoperative bleeding, chylothorax, recurrent nerve palsy, and subphrenic abscess, to say nothing of the fact that 10 of the 26 patients (38%) required postoperative dilations. The experience of Pinotti and associates [4] with 108 transhiatal esophagectomies resulted in an even higher complication rate, as Orringer and Stirling noted in their paper. For these and other reasons, we have adopted a more conservative operative approach to the management of these complex problems. Suppression of acid secretion and alkaline diversion (vagotomy, antrectomy, and Roux-en-Y gastrojejunostomy), accompanied by resection of the distal esophagus and an intrathoracic esophagogastrostomy, has resulted in an approximately 90% rate of improvement [7] with a lower risk than that reported by Orringer and Stirling. Our experience now totals more than 20 patients, and the results continue to be gratifying.

Controversy persists regarding many aspects of therapy for esophageal achalasia; this is especially true for the radical approach proposed by the authors of this important article. As stated at the outset of this editorial, I am in general agreement with their views. However, defining the precise indications for the radical approach and the extent of the operative procedure will have to await the results of further study.

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Does Transfusion Modify the Outcome of Cancer Resections?

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The article in this issue by Moores and associates [1] is the latest in an ever-increasing number of reports emphasizing a possible deleterious effect of perioperative blood transfusions on the prognosis of surgically treated cancer patients. This subject finds its origins in studies on immunity, transplantation, and tumor growth.

The effect of blood transfusions on the integrity of the immune system has been under investigation for many years. It forms part of the basis for awarding the Nobel Prize for Physiology or Medicine to Peter Brian Medawar in 1960 for his work on immunological tolerance [2]. Medawar's original experiments, in which he clarified the rejection phenomenon, included the demonstration that "immunity to skin homografts following massive transfusions of homologous whole blood is either trivial or absent" [3]. In a clinical counterpart of this, Kearns and Reid [4] reported successful homotransplantation of skin from parent to son. Multiple transfusions, which were given to correct severe anemia, may have facilitated graft acceptance—a previously unheard-of phenomenon.

Further investigations proceeded on two main tracks. One deals with renal graft survival. The other, which pertains to the paper by Moores and associates [1], deals with perioperative blood transfusions and cancer prognosis.

The former was spearheaded by the work of Opelz and colleagues. Originally they were studying sensitization (enhanced immunity) of potential graft recipients by blood transfusions, a phenomenon inimical to graft acceptance. They found, paradoxically, that immunosuppression occurred far more often than sensitization, and that patients who had received transfusions had a higher incidence of successful grafts than those who had not. By 1973, preconditioning of renal graft recipients by blood transfusions had become established practice [5].

The second set of studies came on the heels of Gantt's [6] suggestion to use only washed red blood cells in cancer patients. Burrows and Tartter [7], in 1982, published the first report that perioperative blood transfusions might exert a deleterious effect on the prognosis of colon cancer by the same mechanism—immunosuppression—that facilitated renal graft survival. This evoked wide interest, and many reports have since appeared dealing with other forms of cancer including lung, breast, colorectal, soft tissue sarcoma, renal, and head and neck tumors [8].

Most authors agreed with the observations of Burrows and Tartter, but this was not universal. Of four publications on lung cancer, including the paper by Moores and associates, one showed no effect, and similar discrepancies were found in some reports on colorectal and breast cancer and renal cell carcinoma [8].

Meanwhile the investigations on renal transplantation continued. Further refinements, including number of transfusions, proximity to date of operation (preoperative and perioperative), transfusion during the operation itself (peroperative), and various methods of blood preparation (eg, whole blood, packed cells, washed and unwashed, frozen blood), were studied. In addition, cyclosporine A entered the picture in the late 1970s, affecting the process of immunomodulation more than anything before it had.

In 1988, 15 years and about 400 publications later, Opelz [9] noted that "the transfusion effect has suddenly become a hotly debated issue." Whereas in 1982 and 1983, the Collaborative Transplant Study showed that patients who received transfusions had a 15% to 20% higher 1-year graft survival than patients who did not, regardless of whether or not cyclosporine A was used, the same type of analysis for 1984 and 1985 showed only a 5% differential in favor of the patients who received transfusions. This change is still unexplained, but if correct, the hypothesis on which the work on cancer patients is based is greatly weakened. Nevertheless, the observations indicating the deleterious effect of blood transfusions on prognosis of cancer patients appear to be statistically valid or highly suggestive.

Just how does immunosuppression by blood transfusion work? One cannot talk about immunosuppression in general terms, as have the clinical papers on the subject. Immunity is not a single simple phenomenon. Rather, an immunological profile or spectrum exists. Specific antigens cause specific antibodies, usually without cross-reaction to other antigens, as is well shown in immunization of children against specific diseases such as smallpox or pertussis. This mechanism of specificity has not been addressed in any of the papers on transfusion and cancer. It will be necessary to correlate the exact locus on the immunological spectrum where inhibition by transfusions favors accelerated growth and spread of cancer. Also, there may be changes in an individual's immunological profile with the passage of time. Gascon and co-workers [10] have pointed out that "chronic exposure to foreign antigens may be associated with abnormalities of immunologic function but chronically transfused patients do not have the same immunologic profile as reported in some homosexuals and hemophiliacs." Prospective studies of the immunological spectrum and alterations by transfusions alone, transfusions with operation, and operation alone are necessary.

Transfusion techniques and blood-banking practices

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and attitudes toward perioperative transfusions are undergoing extensive reappraisal [11]. No longer is anemia per se an indication for administration of blood unless substantial physiological changes are present. Older concepts about oxygen transport to tissues, wound healing, and "nutritional value" of blood are being abandoned. Experience with patients who are Jehovah's Witnesses demonstrates that severe anemia is well tolerated.

Risks of transfusions are now viewed in a new light, particularly from the standpoint of transmission of viral infections (eg, hepatitis, human immunodeficiency virus). This has led to increased use of autologous blood, which would be a logical way to avoid homologous blood in cancer operations. Also, surgical techniques are almost imperceptibly changing, in part influenced by these new attitudes, to further diminish the need for perioperative blood.

Prognosis in cancer patients is now known to be due to many factors, some newly revealed. For example, recent studies of nuclear DNA have shown that prognosis may be associated with DNA ploidy. This has not been a component of multivariate analyses thus far, and opens an entirely new aspect of tumor prognosis [12].

In conclusion, it may be stated that a phenomenon of some potential importance has been uncovered. But we are really scratching the surface. Intensive work is still required to clarify, validate, and elaborate this phenomenon. In the meanwhile, the avoidance of perioperative blood transfusion in cancer patients is a reasonable objective.

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Cardiac Transplantation in a Private Hospital

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Mr Vice President, members of the Southern Thoracic Surgical Association, and guests. An elocution to such an august body as this is both inspiring and fraught with fear and trepidation. The opportunity to speak to the members of the STSA on any subject in which I have expertise may suggest that I sit down and say nothing. Nevertheless, as I am surely required to occupy a bit of your time, I would like to relate to you the experience with cardiac transplantation of a group of private physicians in a private hospital.

We tend to think of cardiac transplantation as of recent vintage. However, the first reported attempts at experimental cardiac transplantation were by Carrell and Guthrie in 1905. Mann, Demikhov, and others experimented extensively with transplantation prior to the advent of the pump oxygenator. In 1955, Demi was the first to report experiments in which animals survived for a few hours and were solely dependent on the activity of the transplanted heart. By 1960 Lower and Shumway reported success with 5 of 8 consecutive dogs who underwent transplantation and lived for six to 21 days. After many of the technical and physiological problems associated with cardiac transplantation had been overcome, investigators turned their attention to the problem of combating the immune response with chemotherapy.

The first attempted cardiac transplantation for a human patient was undertaken in 1964 when our own Dr Jim Hardy transplanted a chimpanzee heart into a 68-year-old man dying of heart failure. Three years later, on a momentous day in December 1967, Dr C. M. Barnard performed the first human-to-human heart transplantation on a 57-year-old man with ischemic heart disease at the University of Capetown's Groote Schuur Hospital in South Africa.

Following this historic, and first, successful heart transplantation by Dr Barnard, many research institutions began to perform cardiac transplantation. However, the initial enthusiasm for this remarkable operation waned as the problems of acute rejection and infection became apparent and resulted in the deaths of most of the early patients. Despite these problems, four centers—Stanford University and the Medical College of Virginia in the United States, LaPitie in Paris, and the University of Capetown in South Africa—continued with planned programs of heart transplantation.

Two significant events occurred. First, the technique of percutaneous transvenous endomyocardial biopsy, which was introduced by Caves as a method to diagnose acute rejection, contributed to the successful management of transplanted patients because it allowed timely increased immunosuppression or, of equal importance, the avoidance of oversuppression. And second, the introduction of cyclosporin A in the early 1980s, which improved the results of immunosuppression therapy, allowed the procedure of cardiac transplantation to evolve from an experimental to a widely accepted clinical practice; so much so that by early 1985, the results of cardiac transplantation had proved quite successful. Indeed, most major university centers had or were now able to plan cardiac transplantation programs.

Because patients universally prefer to be treated at or near their homes—close to family members and friends—we were convinced that candidates for cardiac transplantation should not be denied this lifesaving treatment because of economic and social adjustments caused by extensive travel or because of their inability to pay for this expensive care. We also believed that a large, church-supported, private tertiary hospital located within a large cardiac referral area should add cardiac transplantation to its armamentarium. Therefore, plans were initiated to begin a cardiac transplantation program at Methodist Hospital in Memphis, Tennessee. Initially, the hospital agreed to support the program with a first-year commitment of up to one-half million dollars for necessary physical plant alterations and equipment, and, most importantly, to supplement the hospital bills of those patients who would be unable to pay.

From January 1986 to September 1988, we evaluated 72 patients for transplantation and 34 were accepted into the program. Twenty-five patients actually underwent orthotopic cardiac transplantation, but 9 died waiting for a donor. The mean age preoperatively was 44 years and ranged from 23 to 60 years. Seventeen patients suffered from ischemic cardiomyopathy, 7 had idiopathic cardiomyopathy, and 1 had valvular heart disease. At the time of transplantation, 6 patients were in the intensive care unit with inotropic or intraaortic balloon pump support, 18 were hospitalized with congestive heart failure, and 7 were at home awaiting cardiac transplantation.

Our operative therapy was standard except for long periods of pump oxygenator support or "payback time" of 30 to 90 minutes after removal of the aortic cross-clamp. Isuprel (isoproterenol) or dopamine was given to insure adequate heart rate. Swan-Ganz catheters and left atrial lines were rarely necessary.

Postoperative care was not different from that given other postoperative cardiac patients except for small doses of Isuprel or dopamine to maintain cardiac rate for a few days, immunosuppressive drugs, and isolation techniques. In addition, our surgical team managed the pa-

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tients' postoperative care, including the management of immunosuppression therapy.

Donor hearts came primarily from the Southeast, with only four from local hospitals. Distant donors required 150- to 860-mile flights. This resulted in ischemic times of one and one-half hours to four hours 33 minutes, or an average ischemic time of three hours. These extended ischemic times had no obvious effect on the early performance of the donor hearts.

The postoperative care of our transplant patients depended on endomyocardial biopsy as the diagnostic procedure of choice for the management of immunosuppressive drugs. All patients underwent endomyocardial biopsy via the right jugular vein on the ninth or tenth postoperative day and at weekly intervals during the first 2 months. Thereafter, bimonthly biopsies for the third and fourth months, and monthly for the fifth and sixth months, were performed. Biopsies were performed every third month for the second 6-month period after transplantation and semiannually thereafter, or as indicated by clinical symptoms. Evidence of acute allograft rejection was most often treated with pulsed steroid therapy. Recurrent or severe rejection was treated with either rabbit antithymocyte serum or OKT3 monoclonal antibody as rescue therapy.

A triple drug immunosuppression therapy regimen was utilized with each patient: cyclosporin A was administered preoperatively in doses of 3 to 8 mg/kg. Postoperatively, cyclosporin was used to maintain trough serum levels of 200 to 400 ng/mL by monoclonal radioimmune assay. This was gradually reduced to maintain serum levels near 100 ng/mL by 12 months and thereafter.

Azathioprine was given in doses of 4 mg/kg preoperatively and 2 mg/kg/day postoperatively, depending on the leukocyte count. The initial dose of steroids was 500 mg of Solu-Medrol (methylprednisolone sodium succinate) intraoperatively, then 125 mg intravenously every 12 hours for three doses. Thereafter prednisone was initially administered in doses of 1 mg/kg/day. This was gradually reduced to 20 mg per day with long-term maintenance lowered to 0.1 to 0.3 mg/kg/day. Antithymocyte serum was given in the immediate postoperative period to each patient for five days.

Fifteen episodes of acute rejection occurred within the first 30 days postoperatively. Each rejection episode was first treated with pulsed steroids. Three of the 15 were subsequently treated with rabbit antithymocyte serum and six have been treated with OKT3, including one in a patient who, because of recurrent rejection, required two courses of OKT3. Our experience in treating these rejection episodes suggests that a recurrent rejection previously treated with OKT3 was subsequently less severe and more easily treated with steroids.

Within this patient population, only three major bacterial infections have occurred. One patient sustained a bilateral empyema requiring prolonged chest tube drainage. A second patient experienced a staphylococcal infection of the sternal wound requiring surgical revision and reconstruction. A third patient sustained a bacteremia as the result of an infected Port-a-cath site. Each of these responded to the usual surgical and antibiotic therapy. There were no viral or fungal infections resulting in clinically significant morbidity or mortality, although almost every patient had minor herpetic infections.

Mortality has been limited to 3 patients. One occurred in the immediate postoperative period due to allograft failure, and there were 2 late deaths due to accelerated graft atherosclerosis. This resulted in a 30-day survival of 96% and a 1-year survival of 91%. As of September 1988, 22 of the 25 transplant patients are alive and doing well up to two and one-half years after transplantation, for an overall survival rate of 88%.

Relevant, current issues with which we struggle include the short supply of donor hearts for transplantation. It is estimated that as many as 10,000 people could benefit annually from cardiac transplantation, whereas fewer than 1,600 procedures were performed last year. Should we use donor hearts from older donors for older recipients now that outlook and risk are improved? And how do we begin to combat the most serious long-term complication of cardiac transplantation, that of accelerated graft atherosclerosis?

Our experience with cardiac transplantation substantiates that this practice can be successful within the confines of a private institution not supplemented by tax dollars. There is nothing extraordinary about our patients, except for the fact that had we not been supported by the hospital, then cardiac transplantation would not have been available to most of them.

There is nothing extraordinary about our approach, except that we have a surgical record that has shown consistent success with cardiac transplantation in a private institution. Hopefully, and with the continued success of our program and others at private hospitals around the nation, cardiac transplantation will be offered to more patients who could not otherwise afford this expensive therapy. Hopefully, more candidates for cardiac transplantation will be able to receive this treatment through private institutions that are closer to their families and friends.

Esophageal Resection for Achalasia: Indications and Results

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Although esophagomyotomy is highly effective as the initial surgical treatment of most patients with achalasia, those with either recurrent symptoms after a previous esophagomyotomy or a megaesophagus do not respond as well to esophagomyotomy. Total thoracic esophagectomy was performed in 26 patients (average age, 49 years) with achalasia. Eighteen had a history of a previous esophagomyotomy, and 18 had a megaesophagus (esophageal diameter of 8 cm or larger). In 24 patients, a transhiatal esophagectomy without thoracotomy was the operative approach; 2 patients required a transthoracic esophagectomy because of intrathoracic adhesions from prior operations. The stomach was used as the esophageal substitute in all patients; it was positioned in the posterior mediastinum, and a cervical anastomosis was performed. Intraoperative blood loss averaged 765 mL. Major postoperative complications included mediastinal bleeding requiring thoracotomy (2), chylothorax (2), and anastomotic leak (1). There were no postoperative deaths. The average postoperative hospital stay was ten days. Follow-up is complete and ranges from 3 to 91 months (average duration, 30 months). All but 1 patient with severe psychiatric disease eat a regular, unrestricted diet without postprandial regurgitation. Early postoperative anastomotic dilation was required in 10 patients. Dumping syndrome has occurred in 5 patients. It is concluded that esophagectomy provides the most reliable treatment of esophageal obstruction, pulmonary complications, and potential late development of carcinoma in the patient with a megaesophagus of achalasia or a failed prior esophagomyotomy and that it is a far better option in these patients than esophagomyotomy, cardioplasty procedures, or limited esophageal resection.

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In North America and Europe, the etiology of achalasia is unknown in most instances, and treatment is directed at relieving the distal esophageal obstruction and not at achieving cure of the disease. The effectiveness of either forceful esophageal dilation or distal esophagomyotomy in relieving dysphagia in the patient with achalasia has been amply demonstrated, and the morbidity of either of these procedures is acceptably low in experienced hands. However, there are circumstances under which neither esophageal dilation nor esophagomyotomy for achalasia can be performed with consistently reliable functional results. These include recurrent neuromotor esophageal obstruction after a previous esophagomyotomy, peptic esophageal stenosis induced by incompetence of the previously disrupted lower esophageal sphincter, and the classic sigmoid-shaped megaesophagus of advanced achalasia, in which esophageal retention in the redundant supradiaphragmatic portion can interfere with emptying even after an adequate esophagomyotomy. These conditions represent a major challenge to the esophageal surgeon, who is called on to utilize alternatives to the traditional distal esophagomyotomy because of anticipated poor results from this operation. This report reviews our experience with 26 such patients with achalasia treated by total thoracic esophagectomy and esophageal substitution with stomach.

Material and Methods

During the past 7 years, we performed esophagectomy in 26 patients with achalasia in whom we anticipated a poor result from a traditional esophagomyotomy. Included in this group were 10 male and 16 female patients ranging in age from 15 to 84 years (average age, 49 years). Eighteen had a megaesophagus, defined as an esophageal diameter of 8 cm or more as measured on the barium swallow examination. The duration of the symptoms of dysphagia and regurgitation ranged from 4 to 55 years and averaged 21 years. Seven patients had experienced no weight loss. In the remaining 19, weight loss ranged from 2.3 to 31.8 kg and averaged 9.53 kg.

Four patients with megaesophagus underwent esophagectomy as the primary esophageal operation; they had had no prior dilation therapy or esophagomyotomy. The remaining 22 patients had each undergone one or more prior esophageal procedures. Esophageal dilations, three pneumatic and three with mercury-filled bougies, had been used in 6 patients. One patient with a megaesophagus that was perforated during attempted pneumatic dilation was treated with an emergent transhiatal esophagectomy and cervical esophagogastric anastomosis. Eighteen patients had undergone a total of 20 distal esophagomyotomies (four transabdominal, 16 transthoracic) and seven hiatal hernia repairs (two Belsey, one

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Collis-Belsey, one abdominal Nissen, one unspecified abdominal, two unspecified thoracic). Among the 18 patients who had a history of a previous esophagomyotomy, the interval between the last esophagomyotomy and the esophagectomy ranged from 6 months to 33 years (average interval, 8 years).

Of our 26 patients, 24 underwent a transhiatal esophagectomy without thoracotomy and 2, a transthoracic esophagectomy. The two transthoracic approaches were necessitated by extenuating circumstances. In 1 of the 2 patients, an attempted transhiatal resection was technically impossible because of the finding of dense periesophageal adhesions associated with two previous esophagomyotomies and one prior hiatal hernia repair. After mobilization of the stomach, the patient was repositioned on the left side, the esophagectomy was completed through a right thoracotomy, and a cervical esophagogastric anastomosis was performed. The other patient had a history of numerous esophageal dilations over the years. At the time of a planned transthoracic esophagomyotomy, extensive periesophageal inflammation and fibrosis from an occult, chronic, contained perforation were found. An esophagomyotomy was not possible. The esophagus was dissected and mobilized from the mediastinum. The left chest was then closed, and the patient was turned supine. Removal of the esophagus and replacement with stomach was then carried out as has been described for a transhiatal esophagectomy. In the remaining 24 patients, a planned transhiatal esophagectomy without thoracotomy was performed.

In all patients, the mobilized stomach was positioned in the posterior mediastinum in the original esophageal bed, and a cervical esophagogastric anastomosis was carried out using a single layer of interrupted 4-0 polyglycolic acid absorbable suture. A pyloromyotomy, nasogastric tube decompression of the intrathoracic stomach for two to three days, and a feeding jejunostomy tube were routine.

Results

Among the 24 patients undergoing transhiatal esophagectomy, intraoperative blood loss ranged from 150 to 3,000 mL (average loss, 765 mL). A chest tube was inserted intraoperatively because of entry into a pleural cavity (right side only, 9; left side only, 6; both sides, 5) in 20 of these 24 patients.

Two of the patients having transhiatal esophagectomy underwent reoperation within 24 hours after esophagectomy because of persistent, slow mediastinal bleeding from an avulsed esophageal artery. In both patients, the bleeding vessel was readily identified and ligated through a right thoracotomy. One of these patients was subsequently found to have a coagulopathy when, after the development of lower extremity weakness following esophagectomy, cervical spinal stenosis, aggravated by extension of the neck at the time of esophagectomy, was diagnosed. A decompressing cervical laminectomy was carried out, and the patient had postoperative bleeding requiring reexploration of that wound as well. A tracheostomy was performed for respiratory insufficiency, and the patient died of pulmonary complications 6 months later. This was the single operation-related death in the series.

Additional complications included chylothorax requiring a thoracotomy for control (2 patients), transient recurrent laryngeal nerve paresis (2 patients), anastomotic leak (1 patient), and subdiaphragmatic abscess (the patient whose esophagectomy was performed emergently for a perforation sustained during balloon dilation). Excluding the patient with spinal stenosis and paraplegia after esophagectomy, postoperative hospitalization ranged from seven to 16 days (average duration, ten days). In 1 patient, a focus of invasive squamous cell carcinoma was found in the resected megaesophagus.

Follow-up is complete for the 25 surviving patients and ranges from 3 to 91 months (average duration, 30 months). All but 1 patient with severe psychiatric disease and chronic depression can eat foods of normal consistency without postprandial regurgitation. Between one and five anastomotic dilations were performed during the first postoperative year in 10 patients who complained of varying degrees of initial cervical dysphagia. Mild nocturnal regurgitation, generally associated with eating before bedtime, has been experienced by 3 patients and severe regurgitation, by the psychiatric patient. No patient has had pulmonary complications secondary to aspiration of gastric contents. Dumping symptoms (postprandial diarrhea and cramping), usually well controlled with diphenoxylate and self-limited, have been experienced by 5 patients. Since the esophagectomy, the weight of 10 patients has stabilized at an average of 11.8 kg greater than the preoperative level, the weight of 12 has stabilized at an average of 5.90 kg less than the preoperative level, and the weight of 3 has remained unchanged.

Comment

The pathophysiology of achalasia is destruction of the Meissner and Auerbach plexuses within the wall of the esophagus, and the degree of neural destruction correlates with the amount of esophageal dilation seen on barium swallow examination [1]. Achalasia is not nearly as prevalent in North America and Europe as it is in South America, where the parasitic protozoan *Trypanosoma cruzi* is endemic. Although the etiology of achalasia in North America and Europe is generally unknown, we have been impressed that the majority of our patients with this disease can antedate the onset of symptoms to a period of major emotional stress in their lives. Years ago, Ellis and Olsen [2] experimentally produced esophageal dilation in cats by bilateral destruction of the dorsal motor nucleus of the vagus nerve. It seems that a central nervous system–mediated process can result in esophageal neural degeneration that has the same ultimate effect as infestation by *T cruzi*, ie, a permanently and irreversibly damaged esophagus, the treatment of which, whether by dilation or operation, is strictly palliative and not curative.

Both forceful dilation and esophagomyotomy have become established as effective means of relieving the esophageal obstruction of achalasia [3]. Recurrent or persistent symptoms after esophagomyotomy have been attributed to (1) an inadequate myotomy, (2) healing of the myotomy, (3) the development of reflux esophagitis, (4) obstruction due to a concomitant fundoplication, (5) an incorrect diagnosis, (6) carcinoma, and (7) the development of a paraesophageal hiatal hernia [4–8]. Regardless of the reason for failure of the original operation, the patient with achalasia requiring reoperation represents a therapeutic challenge, and experience with reoperation for achalasia has been relatively meager; fewer than 300 such patients have been reported [9–14].

The approaches for reoperation for achalasia have been highly variable. They include repeat esophagomyotomy; repeat myotomy with an antireflux procedure; takedown or revision of previous fundoplications; an antireflux procedure alone; cardioplasty; the Thal-Hatafuku procedure [15]; vagotomy, antrectomy, and Roux-en-Y gastrojejunostomy; esophagogastrectomy with esophagogastrostomy; and esophageal resections of varying extent with reconstruction utilizing stomach, jejunum, or colon.

However, the results of these operations have been reported in a relatively subjective, poorly defined fashion, describing "good to excellent" results in 40% to 75% of patients followed for variable intervals ranging from not stated [12] to an average of 10 years [10]. Published reports generally fail to present data on the incidence of persistent regurgitation, pulmonary complications from aspiration, the need for additional dilation therapy or further operations, dietary restrictions, or the amount of weight gain or weight loss after reoperations for achalasia. In a series of 48 reoperations for achalasia, Ellis and associates [9] reported that only two thirds of patients having a repeat myotomy benefited from the surgical intervention, and even poorer results occurred after fundoplication for reflux symptoms. These authors suggested that radical resection procedures might have wider application in patients with achalasia requiring reoperation. We believe that if a repeat myotomy is unsuccessful in one third of patients requiring reoperation, a thoracic esophagectomy and cervical esophagogastric anastomosis provides a much more reliable option.

In North America and Europe, where the incidence of achalasia is relatively low, esophagomyotomy has become the basic surgical approach to this disease, and resection is seldom considered. In South America, on the other hand, where experience with achalasia is far greater, the severity of the disease, as indicated by manometric studies and by radiographic assessment, is an important determinant of the need for resection. Pinotti and associates [16], reporting one of the largest experiences with achalasia in the world, base their treatment on the severity of the disease. They utilize pneumatic dilation in the initial stage (no esophageal dilation) and a transabdominal extramucosal cardiomyectomy with partial fundoplication for the intermediate form (dilation less than 7 cm). However, for advanced achalasia (dilation greater than 7 cm, esophagus usually tortuous, manometrically weak or absent contractions), they believe that resection is the procedure of choice, and they report their results in 108 patients with advanced megaesophagus treated by transmediastinal esophagectomy without thoracotomy. The operative mortality was 3.7%, and complications included pleural effusion (21%), pneumonia (8%), anastomotic leak (8%), pyloromyectomy leak (2%), and tracheal injury (0.9%).

This group [17] has also reported an evaluation of the functional results of esophageal replacement with stomach after transhiatal esophagectomy in 64 patients with advanced achalasia followed from 6 months to 12 years. Sixteen percent complained of regurgitation, primarily at night and requiring them to sleep with the head of the bed slightly elevated, but none had experienced aspiration pneumonia. Slight dysphagia occurred in 6%, all of whom had postoperative anastomotic leaks. Diarrhea occurred in 16% and transient dumping, in 5%. Regarding body weight, 86% gained weight, 8% remained unchanged, and 6% lost weight after the esophagectomy. Slight endoscopic esophagitis was found in 15% and erosive gastritis, in 13%. The fact that fewer of our patients (40%) gained weight after the esophagectomy is most likely a reflection of the better overall nutritional status of North Americans with achalasia compared with South Americans with the parasitic infestation, many of whom are severely cachectic and experience dramatic weight gain postoperatively.

After esophageal replacement with stomach, reduced gastric capacity frequently limits the size of meals, and like patients who have undergone gastric resection for peptic ulcer disease, these patients are instructed to eat smaller, more frequent amounts. Early satiety in the initial months after cervical esophagogastrostomy often resolves spontaneously over the course of the first postoperative year. Because of their inability to overeat, many of these patients lose weight initially, but then gradually regain it and stabilize, though perhaps not back at the preoperative level. These patients, however, are quite satisfied with their ability to eat comfortably and retain a normal diet, and uniformly affirm that their quality of life has been improved.

Ximenes Netto and associates [18], also from South America, draw different conclusions from their experience with 450 patients with Chagas' disease, 67% of whom had advanced megaesophagus. A thoracic myotomy alone was performed in 185 with 0.5% mortality and 92% good results; an abdominal myotomy and Dor fundoplication in 105 with no deaths and 95% good results; a Thal procedure in 108 with 2% mortality and 96% good results; and a subtotal esophagectomy and high intrathoracic esophagogastric anastomosis in 40 patients with 7.5% mortality and only 75% good results. Because of the high morbidity and mortality from the last approach, the group has abandoned resectional therapy as the primary treatment of patients with advanced megaesophagus. It should be emphasized, however, that the frequency of anastomotic leak, sepsis, and postoperative reflux esophagitis after an intrathoracic esophagogastric anastomosis is not comparable with the results that have been reported when the anastomosis is performed in the neck [19, 20].

In our experience, transhiatal esophagectomy without thoracotomy and a properly performed cervical esophagogastric anastomosis [20] can be accomplished safely with acceptable morbidity and good functional results in the patient with megaesophagus of achalasia. The dilated, tortuous esophagus is relatively easily dissected from the mediastinum. With the realization that the aortic esophageal arteries supplying the hypertrophied esophageal muscle in these patients can be larger than normal and therefore more prone to bleeding than in the patient undergoing a transhiatal esophagectomy for other reasons, additional effort should be made to inspect the mediastinum through the diaphragmatic hiatus and to directly clamp and ligate as much of the esophageal blood supply as possible. This can be facilitated by use of narrow, deep retractors placed in either side of the diaphragmatic hiatus or by splitting the anterior diaphragm, as advocated by Pinotti and colleagues [16].

In our experience with more than 400 transhiatal esophagectomies, the 2 patients with achalasia in this series who required a thoracotomy for control of slow mediastinal bleeding within 24 hours after operation are the only patients who have sustained this complication. This does not preclude use of transhiatal esophagectomy in these patients, but rather indicates that additional care to ensure adequate hemostasis must be taken. Furthermore, the need to dissect against the esophageal wall is particularly important in the patient with megaesophagus undergoing transhiatal esophagectomy. The mediastinal pleura surrounding the esophagus is redundant and stretched, conforming to the underlying dilated esophagus, and it is easily torn, thus necessitating a chest tube. The azygos vein, which can be elongated in its course against the dilated esophagus, is potentially more prone to intraoperative injury. Finally, the thoracic duct can be injured as the megaesophagus is mobilized from the mediastinum. Once the esophagus is removed, the mediastinum should be carefully inspected through the hiatus, and if there is any suggestion of lymphatic oozing, the prevertebral soft tissue to the right of the aorta at the diaphragmatic hiatus should be suture-ligated to ensure interruption of the thoracic duct. A postoperative chylothorax after an esophagectomy generally requires a thoracotomy for control [21].

We believe that total thoracic esophagectomy and a cervical esophagogastric anastomosis can be performed in these patients with far more reliable and favorable long-term functional results than can be achieved with the various cardioplasty procedures that have been described. The megaesophagus of advanced achalasia is a functionless organ, which is only a potential source of liability from reflux or retention esophagitis, tracheobronchial aspiration, and the development of cancer. We do not advocate a subtotal thoracic esophagectomy in these patients because this leaves in place some native diseased esophagus. An intrathoracic esophagogastric anastomosis should virtually never be performed for benign disease, as the inevitable reflux esophagitis that follows will result in a poor long-term result. A short-segment distal esophageal jejunal or colonic interposition is simply a more complicated procedure than a cervical esophagogastrostomy. An antrectomy and Roux-en-Y reconstruction for advanced megaesophagus is illogical, as it leaves intact the diseased esophagus while discarding the best alternative organ for esophageal replacement—the stomach!

We think that the relatively poor results from repeat esophagomyotomy or cardioplasty procedures in patients requiring reoperation for achalasia and the potential morbidity from the megaesophagus of advanced achalasia justify resectional therapy and a cervical esophagogastric anastomosis in these patients. The results from this approach are more predictable and reliable than with "conservative" esophagus-sparing procedures, which, in the final analysis, may be a far less satisfactory option because of persistent symptoms and the eventual need for reoperation.

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DISCUSSION

DR CLEMENT A. HIEBERT (Portland, ME): I agree with Dr Orringer on several points. First, his thesis is compellingly simple: why hang on to a pump that does not pump, especially one with a bad valve at its outlet? When operating on the obstruction has been to no avail or has resulted in reflux, perhaps the thing to do is to get rid of the gullet altogether; on occasion, my colleagues and I have done just that with good effect.

Second, I agree that the stomach works rather well as a substitute esophagus, even though you are replacing one atonic sac for another.

Last, I concur with the idea that a high thoracic or cervical esophagogastrostomy reduces the likelihood of serious esophagitis, an observation recorded by Dr Richard Sweet more than 30 years ago.

I respectfully disagree that esophageal resection should be the first operation as it was in 10 of Dr Orringer's patients. Is a caliber of 8 cm or failure of the lower esophageal sphincter to respond to dilation with a mercury-weighted bougie truly an indication for the ultimate operation? Even an incomplete myotomy or one that has caused reflux can ordinarily be rescued with less drastic measures.

My second concern is whether the transhiatal approach is the proper avenue for removing a megaesophagus on those infrequent occasions when it is irrevocably ruined. Dr Orringer, you are the world's expert on this and can do this operation with your eyes closed. (Come to think of it, it is the only thoracic procedure that anyone could do with his eyes closed. The eyes are not even needed.) You have reported your results with customary honesty. All the same, 1 patient died, 4 required reexploration, 2 had transient recurrent laryngeal nerve paresis, and 1 had an anastomotic leak. If you have had such problems after doing the operation more than 200 times for other conditions, do you think less experienced hands should try it for this most difficult problem of refractory achalasia?

DR WILLIAM STEWART LYONS (Alexandria, VA): I will not discuss in detail this interesting and really remarkable paper, but simply will point out that in achalasia, conservative treatment can be very effective. Thirty years ago when I finished my fellowship at the Mayo Clinic, the recommended treatment was hydrostatic dilation as the initial treatment. About 15 years ago, I found on a visit there that the recommended initial treatment had become the Heller procedure.

I asked Art Olsen of the Section of Diseases of the Chest about the change. He acknowledged the previous experience of 80% good results with hydrostatic dilation of the esophagus in achalasia, and I indicated that in my private practice, I was doing just as well, or perhaps a bit better. He thought that the Heller procedure with Bunky Ellis doing it was giving 90% good results. That is the reason for the change, I suppose, but I wonder whether the small improvement justifies choosing a major operation over dilation.

One of my patients, ironically a well-known restaurateur in Washington, DC, had a tortuous and enlarged esophagus. According to the definition of Dr Orringer, the megaesophagus represents the advanced type of achalasia. I dilated the esophagus of this gentleman 25 years ago with good results and again just last year. The megaesophagus particularly is the type that is thought to show indifferent results after dilation. The poor results are due, I believe, not just to the fact that the esophagus is serpentine and slack, but also to the fact that it is difficult to get the dilator in proper position in the cardia.

To help with these difficult cases, I had a special dilator built by Bill Pilling. It is a pneumostatic dilator based on the tapered, weighted 48F Maloney dilator, and under fluoroscopic control, it can be teased into the cardia. The bag itself has radiopaque threads so that one can see it expand and know that it is centered in the cardia. I think that with this instrument, much better results with dilation in the advanced stages of achalasia are obtainable.

DR ORRINGER: Dr Hiebert has used his usual insight to review this work, and he correctly points out that with this operation for megaesophagus, we are replacing one sac with another. The gastric sac, however, serves these patients better, for it empties more efficiently and does not carry a risk of late carcinoma. Long-term follow-up of the functional results of esophageal substitution with stomach, particularly in patients with benign disease, is needed. The fate of the gastric outlet in patients who have had the stomach relocated into the chest will have to be assessed closely. We believe, however, that time will show that these patients are best relieved of the dysphagia and respiratory symptoms from aspiration when the esophagus is removed and replaced with stomach.

I agree completely that esophagomyotomy for achalasia is successful in nearly 90% of patients. But in my practice, and clearly in the practice of surgeons in South America who see this disease more frequently, the results of esophagomyotomy in the patient with megaesophagus are just not as good because of the dependent supradiaphragmatic loop of esophagus that retains food and secretions and interferes with emptying despite the performance of an adequate myotomy. I have no specific predictor of ultimate failure of esophagomyotomy. When I see a tortuous megaesophagus that mechanically has a "sink trap" effect that is not going to be relieved by incising the lower sphincter, I favor an esophagectomy because it provides a more reliable result.

And, Dr Hiebert, I agree that in a series of 26 patients, 4 of whom have required a thoracotomy for complications of the transhiatal approach, one cannot say that this is a low morbidity. There is a "learning curve" that we all have. Our experience with the 2 patients requiring reoperation for mediastinal bleeding alerted us to the fact that extra special care must be taken to obtain hemostasis in the patient with a megaesophagus undergoing a transhiatal esophagectomy. Pinotti, in fact, routinely splits the diaphragm from the hiatus right to the xiphoid in doing a transhiatal esophagectomy, thereby allowing access to the mediastinum and control of bleeding under direct vision. Although we have not incised the diaphragm routinely as advocated by Pinotti, once we have extracted the esophagus from the mediastinum, we place narrow, deep retractors at either side of the diaphragmatic hiatus, and using suction delivered through the cervical incision, we inspect the mediastinum from below as far up as we can see to be certain that there are no bleeding vessels that should be ligated.

Similarly, in our reoperation patients undergoing transhiatal esophagectomy—and these are the ones in whom a postoperative chylothorax will develop because of thoracic duct injury during dissection of mediastinal adhesions—we inspect the mediastinum through the hiatus once the esophagus has been removed. If there is any sign of substantial lymphatic leakage, we suture the prevertebral fascia adjacent to the aorta to ligate the thoracic duct and prevent a chylothorax. I believe that our problems with mediastinal bleeding and chylothorax in this group were a function of an early learning curve experience. Both of these complications are quite rare after transhiatal esophagectomy.

Dr Lyons, I think your conservative approach to megaesophagus in the patient who is asymptomatic is perfectly acceptable. Like you, I would be very conservative in treating a patient who had a dilation for achalasia 25 years ago and has had no complaints until now. I think that your flexible pneumatic dilator is an ingenious device.

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The Society of Thoracic Surgeons is pleased to announce two new membership categories, International and Candidate, with the following qualifications.

International Members: Members of this category shall reside outside the United States and Canada. Their training in this specialty shall be considered equivalent to that of active members. They shall have achieved appropriate certification or recognition of their achievements in this specialty in their country and must devote the majority of their professional efforts in the interests of the specialty. Appropriate documentation of professional achievements shall be provided to the Membership Committee. Members residing in countries other than the United States and Canada elected to membership before October 1, 1988, shall maintain their current status until eligible for Senior Membership or Inactive Status. The dues will be similar to those charged for Active Members.

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Effect of Perioperative Blood Transfusion on Outcome in Patients With Surgically Resected Lung Cancer

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Three hundred thirty patients with non-small cell lung cancer were evaluated to assess the effect of perioperative blood transfusion on overall survival and time to recurrence. One hundred sixty-nine patients received blood products during the perioperative period, and 161 received none. The mean length of follow-up was 3.6 years. There were 90 recurrences, including second primaries, and 99 deaths in the group receiving transfusion; in the group without transfusion, recurrent cancer developed in 74 patients, and 68 died. Survival comparisons, adjusted for stage and cell type using the stratified log-rank statistic, showed significant reduction in survival ($p = 0.007$) for patients receiving transfusion. Time to recurrence was shorter for patients receiving transfusion ($p = 0.035$), but became less significant when adjusted for both cell type and stage ($p = 0.11$). Blood transfusion within the perioperative period appears to have an adverse effect on survival and recurrence in patients undergoing surgical resection for lung cancer.

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The beneficial effect of blood transfusion on kidney allograft survival has been well documented [1–4]. The exact mechanism by which transfusion increases graft survival is not fully understood, but it appears to be related to immunosuppression induced by the transfused blood [5–9]. Sanfilippo and associates [4] showed that improvement in renal graft survival was not related to the method of blood preparation and storage used.

In 1981, Gantt [10] noted the similarity between tumor antigens and histocompatible antigens. He hypothesized that nonspecific immunosuppression induced by blood transfusion might favor tumor growth. Subsequently, there have been several reports of an adverse relationship between blood transfusion and survival after resection of colon cancer [11–14], breast cancer [15], soft tissue sarcoma [16], and lung cancer [17, 18]. However, other authors [19–24] have reported no major adverse effect from transfusion.

This retrospective analysis was undertaken to evaluate the relationship between perioperative blood transfusion and long-term survival in a well-defined patient group treated by surgical resection for non-small cell lung cancer.

Material and Methods

Perioperative blood transfusion was defined as the receipt of any blood product (packed red blood cells, whole blood, or fresh frozen plasma) within 24 hours before or 48 hours after operation. Patients were classified into two groups, those who did and those who did not receive any perioperative blood product, based on careful review of every patient's chart. All patients were taken from the control arms of three separate studies conducted by the North American Lung Cancer Study Group. In these three studies (protocols 771, 773, and 801), each patient had undergone complete resection of his or her tumor, and none had received any perioperative adjuvant therapy. Data on perioperative blood transfusion were available for 330 of the 433 patients who met the eligibility criteria for these studies. There were 169 patients who received blood products and 161 who did not. The mean length of follow-up was 3.6 years. The last statistical analysis of the data was performed in February 1988.

The major statistical end points of the study were time to cancer recurrence, including second primaries, and time to death from any cause. All event times were measured from the time of randomization. The χ^2 statistic was used to test the association between categorical variables and the use of blood products. For continuous variables, the mean values in the blood product groups were compared using the t test. The hazard was estimated as the number of events divided by the total exposure time. Estimates of disease-free survival and survival were made using the method of Kaplan and Meier [25]. Comparison of time-to-event distributions were made using the log-rank statistic [26]. These comparisons were adjusted for the influence of prognostic factors using two methods: the stratified log-rank statistic [27] and the Cox proportional hazards model [28]. The second method was used to assess and adjust for the possible prognostic importance of other factors such as age, white blood cell count, performance status, extent of resection, and serum chemistries. All p values reported are two-sided.

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Table 1. Recurrence[a]

Blood Products	No Recurrence	Recurrence	Total
No	87 (54.0)	74 (46.0)	161
Yes	79 (46.7)	90 (53.3)	169
Total	166	164	330

[a] Numbers in parentheses are percentages.

Table 2. Association Between Use of Blood Products and Survival[a]

Blood Products	Alive	Dead	Total
No	93 (57.8)	68 (42.2)	161
Yes	70 (41.4)	99 (58.6)	169
Total	163	167	330

[a] Numbers in parentheses are percentages.

Results

One hundred sixty-nine patients received perioperative blood products, and 161 did not. Patients who received blood products were found to have a significantly increased incidence of the following: T3 tumors, positive nodes, tumors involving a combination of sites, more extensive resection, non-squamous cell type, more weight loss, higher platelet count, lower hematocrit, and lower creatinine level. All of these factors except the last are commonly associated with more extensive disease. Among those receiving blood products, the average transfusion was 2.8 units.

Recurrent cancer developed in 90 (53.3%) of the 169 patients who received blood products. Of the 161 patients who did not receive blood products, recurrent cancer developed in 74 (46.0%) (Table 1). Seventy (41.4%) of the 169 patients who received transfusions were alive at the time of analysis compared with 93 (57.8%) of the 161 patients who received no blood (Table 2). This apparent effect of blood transfusion on survival and recurrence is illustrated graphically in Figures 1 and 2 without adjustment for extent of disease.

When the overall effect of transfusion on survival was adjusted for TN status and histology using the log-rank statistic, the risk of recurrence for patients receiving blood products did not achieve significance ($p = 0.11$), but a significant increased risk of death persisted ($p = 0.007$) (Tables 3, 4).

Similar results were obtained after adjustment with the Cox proportional hazards regression model. The models attempted to predict time to recurrence and time to death using the blood products group and the following prognostic factors: tumor status, male sex, nonwhite race, combination of sites involved, right side, pneumonectomy, lobectomy, enlarged liver, performance status < 9, non-squamous cell type, white blood cell count, lactate dehydrogenase, calcium, platelet count, creatinine level, percent weight loss, neutrophil count, hematocrit, and age. Except for extent of disease and extent of resection, statistically nonsignificant factors were removed from the model.

In the Cox model, the use of blood products was a significant predictor for recurrence when adjusted for TN status, abnormal alkaline phosphatase, and pneumonectomy ($p = 0.039$) (Table 5). For survival, the use of blood products was a significant predictor for time to death when adjusted for TN status, age, abnormal alkaline phosphatase, and pneumonectomy ($p = 0.006$) (Table 6). The adjusted increased risk of death due to blood transfusion was approximately 1.6-fold. The adjusted risk for recurrence was approximately 1.5-fold. In the simplest terms, this means that transfusion increases the risk of recurrence or death by a factor of approximately 50%, even after adjustment for the more commonly accepted potent prognostic factors.

Comment

The most important factor in predicting outcome in patients with non-small cell lung cancer is TN status. Other prognostic factors such as cell type, elevated leukocyte

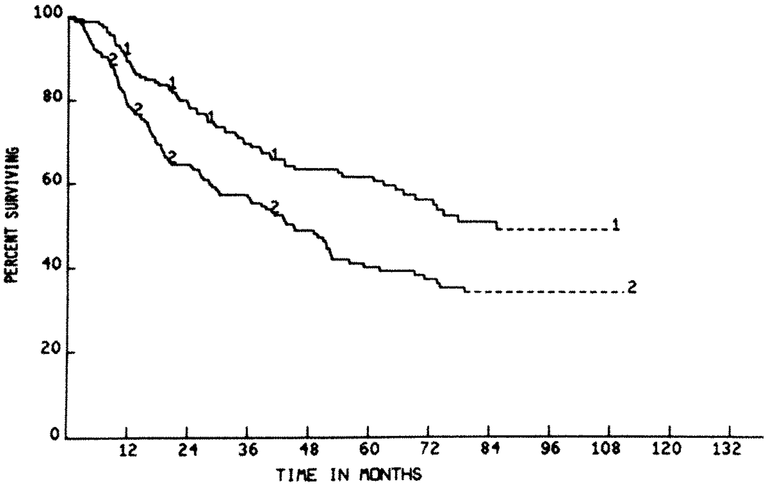

Fig 1. Time to death for 330 eligible control patients in Lung Cancer Study Group protocols 771, 773, and 801. Log-rank p = 0.0013. (1 = patients receiving no blood products [n = 161]; 2 = patients receiving blood products [n = 169].)

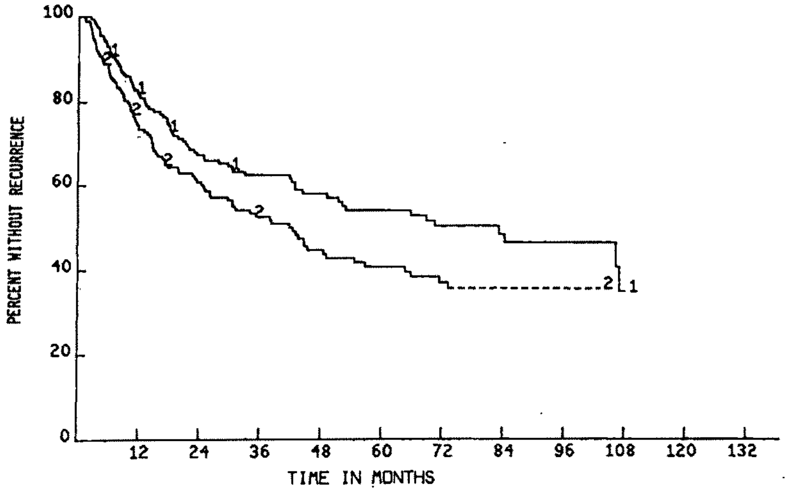

Fig 2. Time to recurrence for 330 eligible control patients in Lung Cancer Study Group protocols 771, 773, and 801. Log-rank p = *0.0353. (1 = patients receiving no blood products [n = 161]; 2 = patients receiving blood products [n = 169].)*

count, and elevated carcinoembryonic antigen levels have been associated with a less favorable outcome among surgically treated patients in previous studies reported by our group [29]. In this study, preoperative values for average platelet count, percent weight loss, and average hematocrit are significantly different in those patients who received blood products. All these may be surrogates for more extensive disease in this group of patients. The significantly lower average creatinine level seen in the transfused group of patients is unexplained.

We have observed a small but significant adverse relationship between perioperative blood transfusion and recurrence and long-term survival in lung cancer patients. The reports of Tartter [17], Hyman [18], and their coworkers support this conclusion, whereas that of Keller and colleagues [24] refutes it. We believe that our estimate of the increased risk of recurrence and death related to perioperative blood transfusion is reliable for several reasons. Our patients met uniform eligibility criteria before participating in their respective studies, and had

Table 3. Events and Hazard Rates for Recurrence

Stratum	Group[a]	No.	Recurrences	Hazard[b]	Hazard Ratio
Squamous cell T1 N0	1	18	4	0.036	1.86
	2	13	4	0.067	
	Total	31	8	0.047	
Squamous cell T1 N1/ T2 N0	1	40	16	0.118	1.43
	2	42	20	0.169	
	Total	82	36	0.142	
Squamous cell II/III	1	26	15	0.255	1.09
	2	64	36	0.279	
	Total	90	51	0.272	
Non-squamous cell T1 N0	1	21	9	0.094	1.15
	2	19	10	0.109	
	Total	40	19	0.101	
Non-squamous cell T1 N1/T2 N0	1	56	30	0.171	1.42
	2	31	20	0.243	
	Total	87	50	0.194	
All strata	1	161	74	0.129	1.44
	2	169	90	0.187	
	Total	330	164	0.155	(p = 0.11)

[a] Group 2 received blood products. [b] This is hazard per patient-year of exposure.

Table 4. Events and Hazard Rates for Survival

Stratum	Group[a]	No.	Deaths	Hazard[b]	Hazard Ratio
Squamous cell T1 N0	1	18	6	0.053	1.62
	2	13	6	0.086	
	Total	31	12	0.065	
Squamous cell T1 N1/ T2 N0	1	40	19	0.120	1.57
	2	42	26	0.189	
	Total	82	45	0.152	
Squamous cell II/III	1	26	13	0.159	1.53
	2	64	39	0.244	
	Total	90	52	0.215	
Non-squamous cell T1 N0	1	21	9	0.087	0.80
	2	19	8	0.070	
	Total	40	17	0.078	
Non-squamous cell T1 N1/T2 N0	1	56	21	0.099	1.87
	2	31	20	0.186	
	Total	87	41	0.128	
All strata	1	161	68	0.101	1.66
	2	169	99	0.168	
	Total	330	167	0.133	(p = 0.007)

[a] Group 2 received blood products. [b] This is hazard per patient-year of exposure.

Table 5. Results of Proportional Hazards Model for All Recurrence, Including Second Primaries

Term[a]	Coefficient	*p* Value	Hazard Ratio
T2	0.6399	<0.001	1.896
T3	0.6364	0.110	1.890
N2	0.6578	0.047	1.931
Abnormal alkaline phosphatase	0.4003	0.040	1.492
Blood products	0.3374	0.039	1.401
Pneumonectomy	0.2219	0.244	1.249

[a] We left T3 and pneumonectomy in because they are such strong prognostic factors.

careful intraoperative staging and independent review of pathological findings. All patients received surgical resection as the only form of initial treatment, and statistical analysis was adjusted for major prognostic factors. As none of these Lung Cancer Study Group studies were designed specifically to detect differences in recurrence and survival due to blood transfusion, it is reasonable to postulate that the differences observed are due to unknown or incompletely controlled prognostic factors including the extent of undetected dissemination of micrometastatic disease.

On the other hand, blood transfusion has been shown to suppress cellular and humoral immunity in both the experimental and clinical setting [5–9]. The exact mechanism is unknown. Francis and associates [30] demonstrated that increased tumor growth after blood transfusion was associated with impaired lymphocyte reactivity to both antigenic and mitogenic stimuli. One possible explanation for this impaired lymphocyte reactivity is the development of soluble suppressor factors in plasma after transfusion [30]. This may be due to elevation in plasma ferritin, which has been demonstrated after transfusion [31]. Ferritin has been shown to suppress lymphocyte function in vitro [32]. In addition, Waymack and colleagues [33] found that allogeneic transfusions increased macrophage production of the strongly immunosuppressive arachidonic acid metabolite prostaglandin E. A second possible explanation for impaired lymphocyte reactivity is induction of suppressor T lymphocytes after transfusion [7, 8]. These experimental observations provide a rational scientific basis for linking an immunosuppressive mechanism to the unfavorable outcome associated with transfusion in our patients.

Table 6. Results of Proportional Hazards Model for Survival

Term	Coefficient	*p* Value	Hazard Ratio
T2	0.5621	0.003	1.754
T3	0.5895	0.124	1.803
N2	0.5629	0.063	1.756
Abnormal alkaline phosphatase	0.4177	0.030	1.518
Age	0.02364	0.015	1.024
Blood products	0.4505	0.006	1.569
Pneumonectomy	0.3988	0.027	1.490

In conclusion, we have demonstrated that perioperative blood transfusion is associated with an increased risk of recurrence and death in patients with lung cancer. This association is explained in part by the fact that patients requiring transfusion tend to have more extensive disease. However, even after adjustment for extent of disease, transfusion remains a significant independent prognostic factor for recurrence and survival. We recommend that surgeons take steps to avoid transfusion in this group of patients when clinically feasible.

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DISCUSSION

DR MICHAEL BURT (New York, NY): In this retrospective review of 330 patients with stages I, II, and III non-small cell lung cancer, the authors have demonstrated that patients who receive blood products have a significant reduction in survival.

Our institute was also interested in the effect of blood transfusion on survival and recurrence rates in patients with non-small cell lung cancer. The patients underwent complete resection, and the results were reported in 1988 in *Cancer*. We reviewed a similar number of patients, 352, with stages I and II non-small cell lung cancer by the new TNM system. Our results differ from those of Moores and associates in that there was no significant difference in either survival or rate of recurrence associated with blood transfusion.

I have two questions for the authors. Was the reduction in survival in those patients given transfusion related to the rate of recurrence? Did a complete or incomplete resection influence the survival in the patients given transfusions?

DR PAUL A. KIRSCHNER (New York, NY): The paper of Dr Moores and associates is still another study on the fascinating and elusive subject of the deleterious effect of perioperative transfusion on the survival of patients with cancer.

Their findings are similar to those of Dr Tartter, Dr Burrows, and myself, which were presented 4 years ago at the New York meeting of The American Association for Thoracic Surgery.

However, to date, despite continued interest in this subject by several groups, the evidence remains only suggestive. Numerous reports—at least 15—have appeared, but no unanimity of opinion exists. In fact, there are some negative reports.

Part of the problem is the lack of uniformity of the case material. For example, in the present study, all stages were considered, whereas in ours, only stage I N0 patients were studied.

To confuse the matter further, the indications for transfusion keep changing—indeed, are becoming stricter—and increasingly the use of autologous blood is entering the picture. What the effect will be, if any, of autologous blood remains to be seen.

Also, in most reports, the level of immunocompetence of patients has not been tested. Immunocompetence can be episodic or irregular, and is subject to many divergent stimuli, only one of which is perioperative transfusion.

Lung cancer, like breast cancer, has a long life history. If we accept the model that it takes 30 doublings for a lung cancer to reach the size of 1 cm^3 and only ten more to kill the patient, we are focusing with perioperative transfusion on a very critical dot in this long life history.

Something, however, is going on. What it is will be found out probably at a molecular level.

There is an immediate practical value of such studies, and that is to restrict blood transfusion to a minimum with resultant lessening of demand on blood banks. Further research is necessary to solve the problem.

DR MOORES: I thank Dr Burt and Dr Kirschner for their discussion.

Dr Burt presented the data from Memorial Sloan-Kettering that were published in *Cancer* in August 1988. In that analysis, as Dr

Burt pointed out, there were 352 patients, the majority of whom were in stage I (305) with a smaller number in stage II (47).

In our data, we saw a hazard ratio of 1.55. Hazard is related to number of events. If there are very few events, there will be no difference. In the Memorial Sloan-Kettering data, there were fewer events than in our data. We included patients in stage II and stage III, and therefore there were more recurrences (events) in our patients.

We calculated the power of the Memorial Sloan-Kettering study to detect a difference at a hazard ratio of 1.5, and found it to be 62%. In comparison, however, our power to predict a difference at a hazard ratio of 1.5 was 73%. I think that had the people from Memorial Sloan-Kettering studied more stage II and stage III tumors, they may well have seen a difference, as there would have been more events.

In response to the question whether incomplete or complete resection had anything to do with survival of the blood transfusion group, all of these patients had complete resection of the tumor, and this was documented by external pathological review.

Notice From the American Board of Thoracic Surgery

The part I (written) examination will be held at the Hyatt-Regency, Dallas/Fort Worth Airport, Dallas TX, on February 4, 1990. The closing date for registration is August 1, 1989.

To be admissible for the part II (oral) examination, a candidate must have successfully completed the part I (written) examination.

A candidate applying for admission to the certifying examination must fulfill all the requirements of the board in force at the time the application is received.

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Porcine Versus Pericardial Bioprostheses: A Comparison of Late Results in 1,593 Patients

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From 1976 to 1988, 1,593 patients underwent valve replacement with a porcine (878 patients) or a pericardial bioprosthesis (715 patients). There were 701 aortic, 678 mitral, and 214 multiple-valve replacements. Follow-up was obtained for 1,559 patients (98%). Early mortality was 9% (79 patients) in the porcine valve group and 5% (37 patients) among patients with a pericardial valve ($p < 0.01$). Late survival after replacement with porcine valves was 80% ± 1% and 62% ± 3% at 5 and 10 years, respectively. With pericardial valves, 5-year survival was 79% ± 2%. Among valve-related complications, rates of freedom from thromboembolism, endocarditis, and hemorrhage after 6 years were similar for both valve groups. Freedom from reoperation at 6 years was also similar after aortic (96% versus 91%) or multiple-valve replacement (95% versus 88%). However, for mitral valve replacement, freedom from reoperation was significantly better with porcine valves than with pericardial valves at 6 years (92% versus 68%; $p < 0.001$). This difference was mainly due to the Ionescu-Shiley valve, which accounted for 83% of primary tissue failures among pericardial bioprostheses implanted in the mitral position (10/12 patients). After 6 years, freedom from primary tissue failure of mitral valves was 92% ± 2% with porcine and 70% ± 11% with pericardial bioprostheses ($p < 0.0001$). The degree of clinical improvement among survivors was similar with both valve types. Thus, in the aortic position, pericardial valves compare with porcine valves up to 6 years, whereas in the mitral position, the durability of the former is significantly less, mainly because of the suboptimal performance of the Ionescu-Shiley pericardial bioprosthesis.

(Ann Thorac Surg 1989;47:352–61)

Porcine and pericardial bioprostheses have both been found suitable valve substitutes for clinical use. However, comparisons between different series are often difficult because group disparities can preclude meaningful conclusions. Porcine bioprostheses have been in continual use since 1976, and pericardial valves of various types have been implanted starting in 1979 at the Montreal Heart Institute. It was therefore of interest to compare two concurrent groups of patients operated on by the same group of surgeons during an overlapping period and followed prospectively with the same clinical criteria. Porcine bioprostheses have been used more extensively and over a longer period than pericardial bioprostheses. Consequently, they can serve as the gold standard for comparative analysis of other bioprostheses, particularly in regard to valve durability, because the main concern with their use remains primary tissue failure, the critical period for which is somewhere between the sixth and 12th year [1–3]. The aim of the present study was to compare pericardial and porcine bioprostheses in terms of patient survival, valve survival, and valve-related complications.

Material and Methods

From 1976 to 1988, 1,593 patients underwent heart valve replacement with a bioprosthesis. One thousand twenty-four Carpentier-Edwards porcine bioprostheses were used in 878 patients (634 standard, 239 improved-annulus, and 151 supraannular models), and 789 pericardial bioprostheses were implanted in 715 patients (316 Ionescu-Shiley, 295 Carpentier-Edwards, and 178 Mitroflow valves). There were 808 male and 785 female patients aged 13 to 80 years. The male to female ratio was 0.93 in the porcine group compared with 1.16 in the pericardial group ($p < 0.05$). The latter group included a greater proportion of patients older than 60 years (Fig 1), and the mean age (57 ± 12 years [mean ± standard deviation]) was significantly higher than that of patients in the porcine group (54 ± 12 years) ($p < 0.01$).

Preoperatively, 89 patients (5.6%) were in New York Heart Association functional class I, 551 (34.6%) were in class II, 829 (52%) were in class III, and 124 (7.8%) were in class IV. In the porcine valve group, 61.8% (543 patients) were in functional class III or IV compared with 57.3% (410 patients) of the pericardial valve patients, a difference that is not significant ($p > 0.05$). Aortic stenosis was more frequent in the pericardial valve group ($p < 0.0001$), whereas aortic regurgitation ($p < 0.0001$), mitral stenosis, and mitral regurgitation were seen more often in the porcine valve patients (Table 1). A cardiac operation had been done previously in 359 patients (22.5%), 189 in the porcine valve group (21.5%) and 170 in the pericardial

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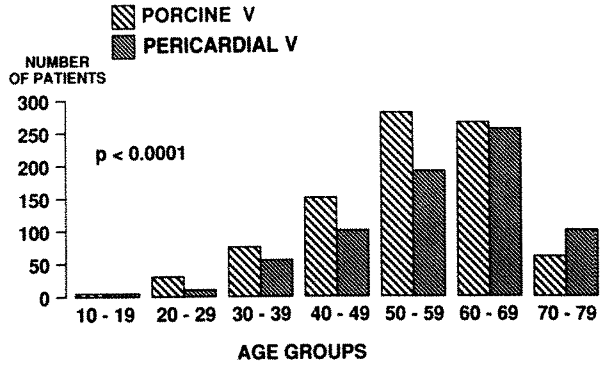

Fig 1. Patient distribution by age groups indicates a preponderance of porcine valves (V) in patients less than 60 years old and a majority of pericardial valves in patients older than 70 years.

valve group (23.8%) ($p > 0.05$). However, failure of a valve prosthesis was the indication for operation more often in the pericardial valve group (67 patients, 9.4%) than in the porcine valve group (24 patients, 2.7%) ($p < 0.0001$).

A Carpentier-Edwards porcine bioprosthesis was used for isolated aortic valve replacement (AVR) in 331 patients (37.7%), for isolated mitral valve replacement (MVR) in 419 patients (47.7%), and for multiple-valve replacement (MR) in 128 patients (14.6%). A pericardial bioprosthesis was implanted in 370 patients (51.7%) for AVR, in 259 (36.2%) for MVR, and in 86 (12%) for MR. The difference between the two groups was significant ($p < 0.0001$). Coronary artery bypass grafting was associated with the valve procedure in 135 (15.4%) of the patients with a porcine valve and 155 (21.7%) of those with a pericardial bioprosthesis ($p < 0.01$). Associated surgical procedures are listed in Table 2.

Table 2. Associated Surgical Procedures

Procedure	Porcine Valve Group No.	%	Pericardial Valve Group No.	%
Coronary artery bypass grafting	135	15.4	155	21.7
Valve repair	77	8.8	44	6.2
Enlargement aortoplasty	10	1.1	13	1.8
Bentall procedure	4	0.5	3	0.4
Resection of left ventricular aneurysm	3	0.3	13	1.8
Closure of ventricular septal defect	2	0.2	5	0.7
Postoperative intraaortic balloon pumping	33	3.8	19	2.7

Patients were followed on a yearly basis either at the outpatient clinic or through their own physician. Overall, 34 patients were lost to follow-up, 19 (2.16%) in the porcine valve group and 15 (2.10%) in the pericardial valve group, for a global follow-up of 97.9%. The duration of follow-up of patients with a porcine bioprosthesis averaged 74 months, totaling 4,899 patient-years, compared with 34 months and 1,936 patient-years for the pericardial valve group.

At the last follow-up visit, 28.4% (227 patients) of patients with porcine valves and 26% (176 patients) of those with pericardial valves were on a regimen of anticoagulation therapy, and antiplatelet agents were administered to 11.5% (92 patients) and 19.9% (135 patients) of the patients, respectively.

Definitions

An embolic episode was defined as any new neurological deficit, either transient or permanent, or any suggestive symptom, as well as all events of clinically detectable noncerebrovascular embolism, excluding perioperative cerebrovascular accidents (first week).

Endocarditis was defined as any systemic infection with positive hemoculture or signs of infection of the prosthesis at reoperation or autopsy, including the early postoperative period.

Table 1. Preoperative Diagnosis

Diagnosis	Porcine Valve Group (n = 878) No.	%	Pericardial Valve Group (n = 715) No.	%	p Value[a]
Aortic valve					<0.0001
Stenosis	189	21.5	260	36.4	
Regurgitation	228	26	141	19.7	
Mixed	21	2.4	26	3.6	
Mitral valve					NS
Stenosis	315	35.9	195	27.3	
Regurgitation	144	16.4	91	12.7	
Mixed	80	9.1	33	4.6	
Prosthetic valve dysfunction	24	2.7	67	9.4	<0.0001

[a] Porcine valve group versus pericardial valve group.

NS = not significant.

Periprosthetic leak was defined as any major valvular regurgitation demonstrated at heart catheterization (>grade 2/4), reoperation, or autopsy.

Hemorrhage was considered a complication whenever treatment or hospitalization of a patient on a regimen of anticoagulant therapy was required.

Primary tissue failure of a bioprosthesis included dysfunction with regurgitation due to leaflet tear, stretching, or creeping of the stent, or valvular obstruction by leaflet fibrosis or calcification.

Valve-related complications were defined as any complications caused by the presence of a heart valve prosthesis. All late deaths from any cardiac-related causes were considered valve-related deaths.

Valve survival was computed from freedom from valve-related death (cardiac-related death) and from reoperation for replacement or repair of a prosthesis.

Data Analysis

Student's t test and the χ^2 test were used for statistical analysis of the data. Results are expressed either as linearized incidence or using the life-table method with standard error of the mean. The accepted level of significance was 95%.

Results

Survival

There were 79 early deaths among the porcine valve group, a 30-day mortality of 9.0%, and 37 deaths in the pericardial valve group, a 30-day mortality of 5.2% ($p < 0.01$). The respective early mortality rates were 6.6% (22 patients) and 3.8% (14 patients) for AVR, 8.8% (37 patients) and 5.4% (14 patients) for MVR, and 15.6% (20 patients) and 10.5% (9 patients) for MR. None of these differences were significant ($p > 0.05$).

Among patients with a porcine valve, there were 141 late deaths compared with 68 in the pericardial valve group, giving linearized late mortality rates of 2.9%/patient-year and 3.5%/patient-year, respectively. The overall survival curves of both groups were similar, as were those for AVR, MVR, and MR separately (Figure 2). Global actuarial survival of patients with porcine valves was 80% ± 1% at 5 years and 62% ± 3% at 10 years, whereas that of patients with pericardial valves was 79% ± 2% after 5 years. Causes of death are shown in Table 3. The most frequent cause in both groups was congestive heart failure (32% and 30%, respectively). A noncardiac cause was responsible for 11% of deaths in each of the two groups. However, autopsy was done in slightly less than half of the patients who died in each group.

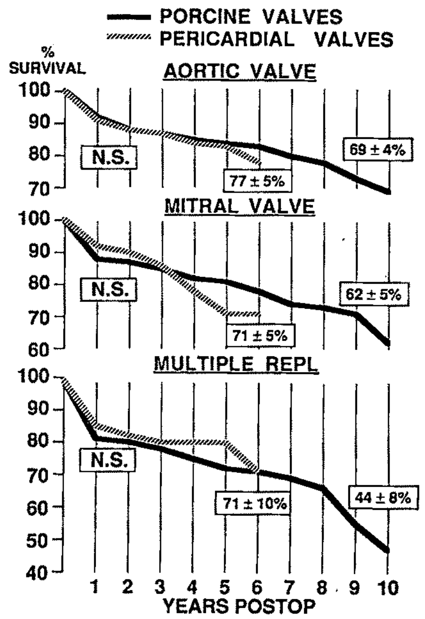

Fig 2. Actuarial survival curves for porcine valve and pericardial valve patients indicate that the differences are not significant (N.S.). (REPL = *replacements.*)

Complications

THROMBOEMBOLISM. With the porcine valve, there were 53 thromboembolic episodes (1.08%/patient-year): seven fatal, 14 with residual deficits, and 32 minor accidents. In the group of patients with pericardial bioprostheses, 39 sustained this complication (2.01%/patient-year); 4 died, 11 had permanent deficits, and 24 were without permanent deficits. Although the linearized incidence was higher with pericardial valves in AVR, MVR, and MR (Table 4), the actuarial curves of freedom from thromboembolism were not significantly different (Fig 3). Freedom rates at 10 years for porcine and at 6 years for pericardial valves were 96% ± 1% and 94% ± 2% after AVR, 89% ± 2% and 89% ± 3% after MVR, and 86% ± 5% and 88% ± 4% after MR, respectively. There were three cases of valve thrombosis, two in the porcine valve group (one aortic and one mitral) and one in the pericardial valve group (aortic). The patient with the porcine mitral valve

Table 3. Causes of Death[a]

Cause	Porcine Valve Group (n = 220)	Pericardial Valve Group (n = 105)
Congestive heart failure	70	31
Sudden death	33	8
Myocardial infarction	25	12
Arrhythmias	21	9
Reoperation	19	9
Perioperative hemorrhage	11	4
Cerebrovascular accident	6	5
Endocarditis	3	6
Hemorrhage due to anticoagulants	4	3
Valve failure	2	2
Valve thrombosis	1	0
Unknown	2	4
Noncardiac	23	12

[a] Autopsy was performed on 101 patients (45.9%) in the porcine valve group and 52 (49.5%) in the pericardial valve group.

Table 4. Valve-Related Complications

	Porcine Valve Group				Pericardial Valve Group			
Complication	AVR	MVR	MR	Total	AVR	MVR	MR	Total
Thromboembolism								
Minor	4	21	7	32	9	11	4	24
Major	5	5	4	14	3	5	3	11
Fatal	2	5	0	7	2	1	1	4
Total	11	31	11	53	14	17	8	39
%/patient-year	0.56	1.37	1.64	1.08	1.36	2.52	3.5	2.01
Endocarditis								
Fatal	3	0	2	5	5	3	0	8
Total	11	8	4	23	15	5	7	27
%/patient-year	0.56	0.35	0.6	0.47	1.45	0.74	3.06	1.39
Hemorrhage								
Fatal	1	3	0	4	0	2	0	2
Total	1	15	1	17	2	4	2	8
%/patient-year	0.05	0.66	0.15	0.35	0.19	0.59	0.88	0.41
Reoperation								
Fatal	6	6	7	19	6	2	1	9
Total	25	55	25	105	16	17	7	40
%/patient-year	1.27	2.43	3.73	2.14	1.55	2.52	3.06	2.07
Primary tissue failure								
Total	20	54	24	98	4	12	3	19
%/patient-year	1.02	2.39	3.58	2.00	0.39	1.77	1.31	0.98
All complications								
Total	47	111	41	199	43	41	21	105
%/patient-year	2.39	4.9	6.11	4.06	4.16	6.22	8.75	5.42

AVR = aortic valve replacement; MR = multiple-valve replacement; MVR = mitral valve replacement.

died, whereas the 2 with thrombosed aortic valves underwent reoperation successfully.

ENDOCARDITIS. Twenty-three episodes of endocarditis occurred in patients with porcine valves (0.47%/patient-year) compared with 27 among those with pericardial bioprostheses (1.39%/patient-year). The linearized rates were higher with the latter valve in all positions (see Table 4). However, freedom-rate curves were not significantly different for AVR (92% ± 4% freedom at 6 years for pericardial valves and 95% ± 2% freedom at 10 years for porcine valves) and MVR (97% ± 1% freedom for pericardial valves at 6 years and 97% ± 1% for porcine valves at 10 years). In the MR group, endocarditis was significantly more frequent with pericardial than with porcine valves; respective freedom rates were 88% ± 5% at 6 years and 96% ± 3% at 10 years ($p < 0.05$) (Fig 4).

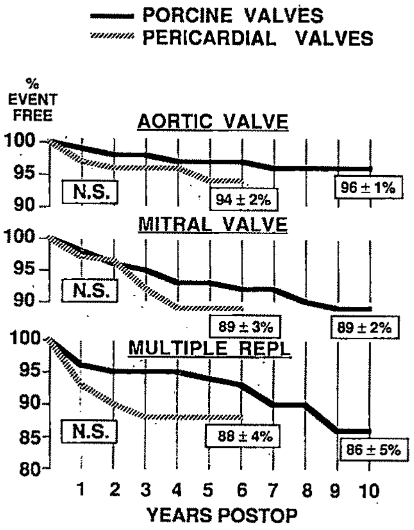

Fig 3. Freedom from thromboembolic complications. (N.S. = *not significant;* REPL = *replacements.)*

HEMORRHAGE. Patients with porcine valves sustained 17 hemorrhagic accidents (0.35%/patient-year), 4 of which were fatal, compared with 8 in the pericardial valve group (0.41%/patient-year), 2 of which were fatal accidents. Only three (12%) of all 25 episodes occurred after isolated AVR.

HEMOLYSIS. No clinically significant hemolysis was detected with any of these bioprostheses in the absence of major valve dysfunction.

REOPERATION. Reoperation was performed in 105 patients with a porcine bioprosthesis (2.14%/patient-year) and in

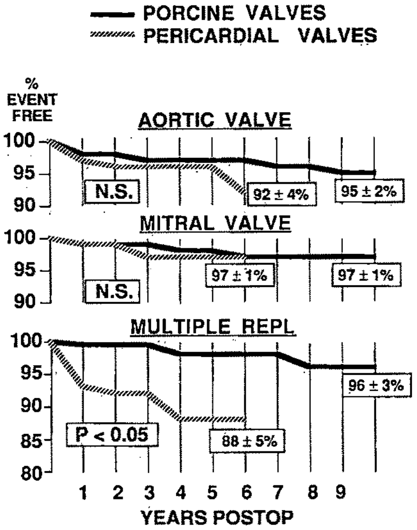

Fig 4. Freedom from endocarditis. (N.S. = *not significant;* REPL = *replacements.)*

Table 5. Indications for Reoperation

	Porcine Valve Group		Pericardial Valve Group	
Indication	No.	%	No.	%
Leaflet tear or stretching	72	68.6	17	42.5
Prosthetic valve obstruction	20	19.0	2	5.0
Paravalvular leak	8	7.6	8	20
Active endocarditis	4	3.8	12	30
Valve thrombosis	1	0.9	1	2.5
Total	105		40	

40 patients with a pericardial valve (2.07%/patient-year). With either type of prosthesis, the linearized rate of reoperation was higher after MVR or MR than after isolated AVR by a ratio of almost 2 to 1 (see Table 4). Freedom from reoperation for any cause was 96% ± 1% and 83% ± 5% at 6 and 10 years, respectively, with porcine aortic valves and 91% ± 4% at 6 years with pericardial valves ($p > 0.05$) (Fig 5). In the mitral position, freedom rates for porcine valves were 92% ± 2% at 6 years and 53% ± 6% at 10 years compared with 68% ± 11% at 6 years with pericardial valves ($p < 0.001$). After MR, freedom from reoperation was 95% ± 2% and 41% ± 9% at 6 and 10 years, respectively, with porcine valves and 88% ± 4% at 6 years with pericardial valves ($p > 0.05$). The mortality rate of this complication was 18.1% (19 patients) with porcine valves and 22.5% (9 patients) with pericardial valves.

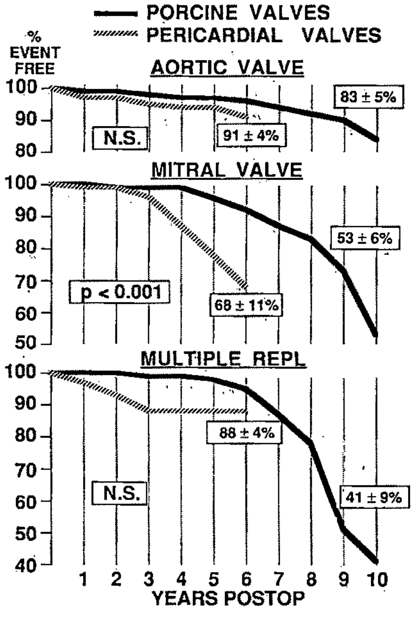

Fig 5. Freedom from reoperation due to all causes. (N.S. = *not significant;* REPL = *replacements.)*

Indications for reoperation are shown in Table 5. Primary tissue failure was responsible for 88% (92 patients) of reoperations in the porcine group and for 48% (19 patients) of reoperation among patients with a pericardial valve ($p < 0.0001$). A much higher rate of reoperation was due to active prosthetic valve endocarditis in the latter group (12 patients, 30%) than in the former (4 patients, 3.8%) ($p < 0.0001$), reflecting the higher incidence of endocarditis in the pericardial valve group (1.39%/patient-year versus 0.47%/patient-year).

VALVE DYSFUNCTION. In addition to those who underwent reoperation, 6 patients with a porcine valve (0.12%/patient-year) were found to have major valve dysfunction, 2 of whom died. In the pericardial valve group, a diagnosis of valve dysfunction was established at autopsy in 2 additional patients (0.10%/patient-year).

Overall, primary tissue failure occurred in 98 porcine valves (2.0%/patient-year) and in 19 pericardial valves (0.98%/patient-year) ($p < 0.01$). With both bioprostheses, the incidence was higher among mitral than aortic valves (see Table 4). After 6 years, the actuarial freedom rate was similar for both valves in the aortic position (98% ± 1% and 94% ± 4%; $p > 0.05$), as well as for patients with MR (95% ± 2% and 94% ± 4%), but there was a significant difference between the two curves for mitral bioprostheses (92% ± 2% versus 70% ± 11% at 6 years; $p < 0.0001$) (Fig 6). After 10 years, freedom from primary tissue failure for porcine valves was 82% ± 5% for AVR, 54% ± 6% for MVR, and 42% ± 9% for MR.

Freedom from all valve-related complications after 6 years was significantly better with porcine than pericardial prostheses, with respective rates of 90% ± 2% and 79% ± 5% for AVR ($p = 0.05$), 80% ± 2% and 56% ± 10% for MVR ($p < 0.0001$), and 85% ± 4% and 69% ± 6% for MR ($p < 0.05$) (Fig 7). As for valve survival at 6 years, it was slightly better with porcine valves in AVR (89% ± 2% versus 82% ± 4%) and MR (84% ± 4% versus 74% ± 10%), although not significantly so. However, in the mitral position, porcine valves survived significantly

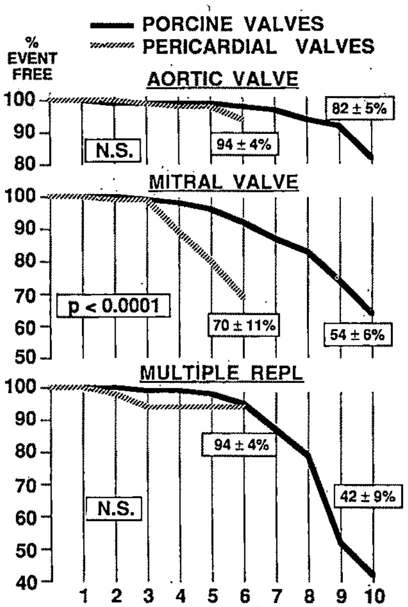

Fig 6. Freedom from primary tissue failure. (N.S. = *not significant;* REPL = *replacements.)*

longer than pericardial bioprostheses (80% ± 2% versus 62% ± 10% at 6 years; $p < 0.01$) (Fig 8).

Among the three different types of pericardial bioprosthesis implanted in this series, the Ionescu-Shiley valve accounted for 58% of reoperations (23/40 patients) and for 63% of primary tissue failures of the valve (12/19 patients). The higher complication rate in the pericardial group was almost completely due to the use of this prosthesis in the mitral position; the Ionescu-Shiley valve was responsible for 65% of reoperations (11/17 patients) and for 83% of primary tissue failure (10/12 patients) of mitral pericardial bioprostheses (Fig 9).

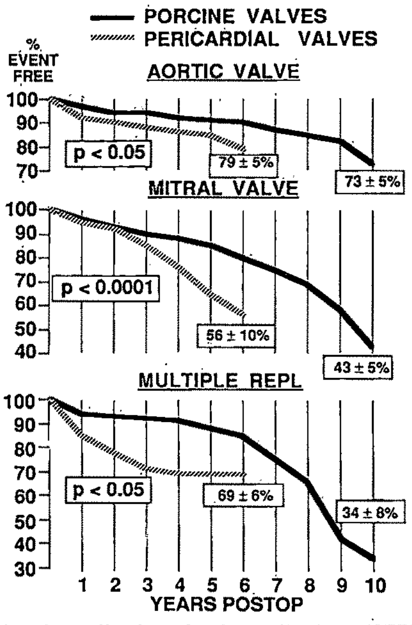

Fig 7. Freedom from all valve-related complications. (REPL = *replacements.)*

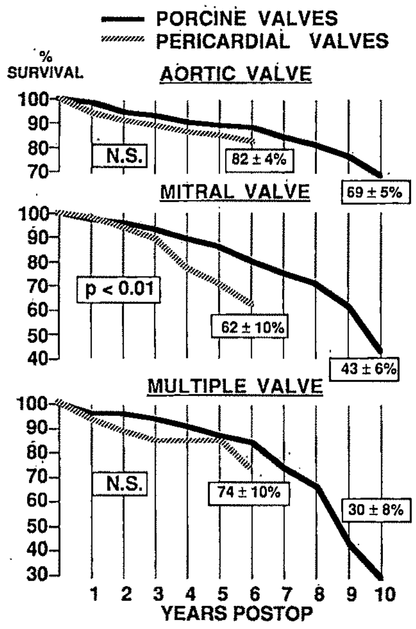

Fig 8. Actuarial valve survival (freedom from cardiac-related death and from reoperation). (N.S. = *not significant.)*

CLINICAL IMPROVEMENT. Of the 573 patients with porcine valves who survived without reoperation, 94% (540 patients) remained in functional class I or II at their last follow-up visit an average of 79 months postoperatively. With pericardial valves, 98% (568 patients) of the 581 survivors without reoperation were in class I or II after an average follow-up of 36 months. Overall, only 46 patients (4%) remained markedly incapacitated (class III or IV) when last seen (Fig 10).

Comment

The choice of a valve substitute remains a matter of controversy. Comparing various series in the literature can be misleading because of differences in patient choice, management, or follow-up. In addition, nonconcurrent studies can introduce a bias favoring the more recent prosthesis. Two studies [4, 5] published in 1987 compared

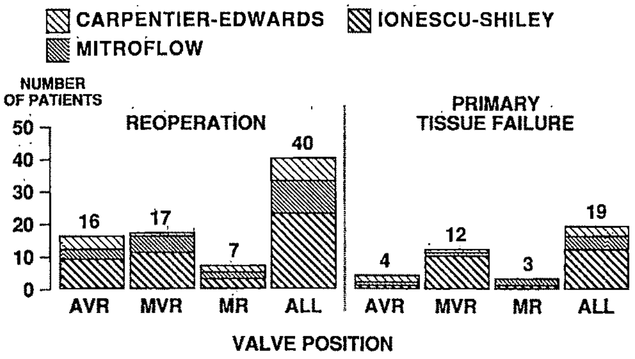

Fig 9. Reoperation and primary tissue failure of pericardial bioprostheses according to valve type and position. (AVR = *aortic valve replacement;* MR = *multiple-valve replacement;* MVR = *mitral valve replacement.)*

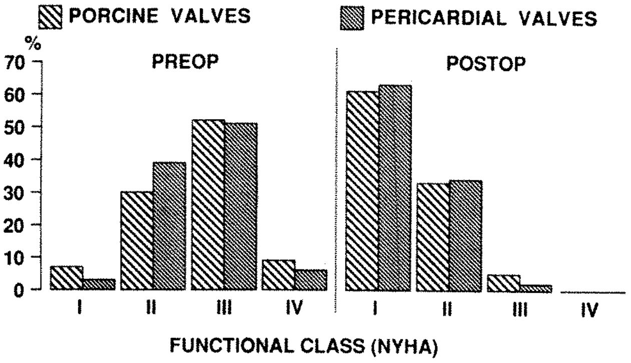

*Fig 10. New York Heart Association (*NYHA*) functional class preoperatively and postoperatively for each group.*

biological and mechanical valves. After 5 years, the probability of remaining free from valve-related complications was significantly higher with bioprostheses than with mechanical valves in both the aortic and mitral positions [4]. This difference was mainly due to the increased incidence of major though nonfatal episodes of bleeding with the latter type. At 10 years, no significant differences in the overall valve-related mortality and morbidity were found between the two types of valves [5]. Although mechanical valves had a greater incidence of thromboembolism and reoperation for perivalvular leak, bioprostheses had a higher rate of primary valve failure. These studies suggest that there is still an important place for bioprostheses in clinical use, despite present evidence indicating that they will all fail with time.

In the present series, the two groups of patients overlap over most of the study period, although a majority of porcine valves were implanted before 1982 and most pericardial valves were used during the last 6 years. This may partly account for the higher early mortality (9%) in the porcine valve group compared with the pericardial valve group (5.2%). However, overall patient survival after up to 6 years was similar in the two groups. Our 5-year and 10-year survivals of 80% and 62%, respectively, compare with those of others [3, 5]. There was no difference in late survival between the two groups, whatever the valve position.

Completeness of follow-up was excellent, as postoperative evolution status was known for 97.9% of all patients, and lost patients represented a similar proportion in each group. Among late survivors, excellent clinical improvement was obtained after valve replacement with either type after an average follow-up of 6.5 years with porcine valves and 3 years with pericardial valves.

Although there was a tendency for a higher incidence of thromboembolic events with pericardial valves in all positions, freedom curves did not reach significance up to 6 years. The proportion of patients receiving anticoagulants was similar, but that of patients with antiplatelet agents was greater among pericardial patients. On the other hand, the linearized rate of hemorrhagic complications was strikingly low with both valves (0.35%/patient-year and 0.41%/patient-year). The overall rate for those two complications was 1.4%/patient-year for porcine valves and 2.4%/patient-year for pericardial valves, which is much lower than that reported with most mechanical valves [6–9].

Endocarditis had a low incidence with both valves, although it was significantly more common among patients who underwent MR with pericardial prostheses. A more aggressive attitude toward early surgical treatment of complicated endocarditis in recent years might partly account for this difference [10]. The higher rate of reoperation because of endocarditis among pericardial valve patients is probably also the result of this therapeutic trend. With the exception of this latter group, freedom from endocarditis after 5 years was 95% or higher with both types of valves, and it remained so up to 10 years with porcine bioprostheses.

No clinically significant hemolysis occurred when valve function was normal in the present study. In a previous analysis of the Carpentier-Edwards pericardial valve [11], only trivial biochemical signs of hemolysis were found, whereas a slightly higher degree of hemolysis was reported with the Ionescu-Shiley valve, although hemolysis remained at subclinical levels [12].

Of all valve-related complications, degeneration and failure of bioprostheses remains the major issue at stake. Although freedom from reoperation was similar for porcine and pericardial valves in the aortic position up to 6 years postoperatively, in the mitral position it remained consistently better with porcine valves after the third year. With MR, there was also a tendency for less reoperation with porcine valves but the difference did not reach significance. Primary tissue failure was responsible for 88% of reoperations in the porcine valve group and 48% in the pericardial valve group. However, a much higher proportion of the latter group underwent reoperation because of endocarditis, 30% in contrast to less than 4%, particularly among patients who underwent MR. With either type, reoperation was less likely after AVR than MVR, and at 10 years, freedom from reoperation was 83% and 53%, respectively, after replacement with porcine bioprostheses. Whereas the actuarial freedom curves for the aortic position showed a constant but progressive fall, mitral valve curves indicated a steeper decline starting at the 3-year mark for pericardial valves and at 8 years for porcine valves.

Freedom curves for primary tissue failure of porcine valves were very similar to those for reoperation because valve failure was responsible for most reoperations. Curves of primary failure of pericardial valves were not different from those for porcine valves in the aortic position and with MR. This is in contrast with the results of a study comparing Ionescu-Shiley pericardial with Hancock porcine aortic valves, which indicate a greater tendency to tissue failure with the former, starting at the sixth year [1]. However, in the present study, Ionescu-Shiley valves accounted for only one third of AVRs in the pericardial group, which may explain this discrepancy. In a previous study [11] of Carpentier-Edwards aortic pericardial valves, no primary tissue failure occurred up to 5 years and freedom from reoperation for any cause was 98%. On the other hand, pericardial valves showed a much higher degree of degeneration in the mitral position, with a freedom rate after 6 years of 70% compared with 92% with porcine prostheses. The Ionescu-Shiley pericardial valve was responsible for 83% of cases of mitral valve failure.

Early degeneration of Ionescu-Shiley and Hancock pericardial valves has been found to occur at alarming rates, leading to their withdrawal from clinical use [13–16]. In an animal model, pericardial valves (Ionescu-Shiley and Mitroflow) were shown to develop calcification more extensively and more rapidly than Carpentier-Edwards and Hancock porcine valves [17]. An in vitro study [18] stressed the role of mechanical and design factors in the genesis of tissue degeneration, pericardial valves failing mainly because of damage sustained during valve closure, whereas porcine valves appeared to be damaged mainly during the opening phase of the cardiac cycle. Whereas calcification of porcine valves appears to be related to areas of maximum stress on the leaflet [19], leaflet tears of Ionescu-Shiley pericardial valves are mostly related to the holding commissural suture at the summit of the stent [20, 21].

Our long-term results with the Carpentier-Edwards porcine bioprosthesis are similar to those of others with either the same valve or the Hancock porcine valve [3, 22, 23], with an overall valve survival rate of 88% ± 1% and 51% ± 3% after 5 and 10 years, respectively. Reported rates of valve survival with frozen aortic homografts range from 70% to approximately 85% at 5 years and from 57% to 59% after 10 years [24, 25]. Although there is a tendency for survival of porcine valves to be better than that of pericardial valves in all positions, it reaches significance only with mitral prostheses. However, if freedom from all valve-related complications is considered, results are significantly better with the former in all positions.

In conclusion, the Carpentier-Edwards porcine bioprosthesis appears to perform better than pericardial valves after the third to fourth year. This is particularly true in terms of the durability of mitral valves. However, the differences between the two types of bioprostheses appear to be mostly due to early tissue degeneration of the Ionescu-Shiley pericardial valve. A more detailed analysis of each type of pericardial valve should be undertaken to clarify its specific performance individually.

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DISCUSSION

DR GEORGE J. REUL (Houston, TX): I congratulate Dr Pelletier and the group at the Montreal Heart Institute for a very concise analysis completing an important chapter of valve surgery.

Our experience with the Ionescu-Shiley pericardial valve at the Texas Heart Institute closely parallels their experience with the pericardial valve. The major difference was in freedom from reoperation in the mitral valve and aortic valve patients. At 6 years, freedom from reoperation was the same in the aortic valve and mitral valve patients, and at 7 years it was higher in our aortic valve group. Dr Pelletier has shown that the reoperation rate was higher in the mitral valve patients at 4 years. Furthermore, at 6 to 7 years there was almost a 10% increase in our reoperation rate.

The reason that aortic valve reoperation was required more frequently than mitral valve reoperation in our patients was because of the mode of tissue failure. Dr Pelletier has shown that leaflet disruption was the major mode of tissue failure. Most of the follow-up data of others have shown that the pericardial valve calcifies at a faster rate than the porcine valve. Our increased incidence of aortic valve reoperation was mostly due to calcification. Under the age of 30 years, the mean time for occurrence of calcification was almost 3.5 years, whereas in the older age group, the mean time of calcification was about 5 years. Because of the older mean age in Dr Pelletier's series, the aortic valve failure rate will probably equal the mitral valve failure with more time for follow-up.

Because of bias in patient selection, some of Dr Pelletier's comparisons may not be valid. The pericardial valve was used more frequently in patients with aortic stenosis and with prosthetic valve failure. Why did the surgeon choose the pericardial valve in preference to the porcine valve? Is this because a pericardial valve can be used in a patient with a smaller annulus compared with the porcine valve? Only 8% of the patients were functional class IV and only about 2% of the patients had enlargement procedures on the annulus. Were mechanical valves used in other patients not included during this time frame?

Another area of concern was the higher incidence of endocarditis in the pericardial valve compared with the porcine valve. Our incidence of endocarditis with the Ionescu-Shiley valve was exactly the same as their incidence of endocarditis with the porcine valve, that is, 0.4%/patient-year. Was there a higher incidence of endocarditis in the pericardial valve patients because endocarditis was present preoperatively more frequently in the pericardial valve patients?

It would be of interest to stratify the results in the pericardial group according to valve type. Do you have enough data to show that the Ionescu-Shiley valve is different from the Carpentier-Edwards valve and the other pericardial valves utilized?

Finally, a question that we'd all like you to answer based on these data is whether or not there is any indication at the present time for the use of a pericardial valve.

DR ROBERT W. M. FRATER (Bronx, NY): I'm a great admirer of Dr Pelletier's work, and I'm very glad that in his last sentence he made the point that it is necessary to distinguish between different kinds of pericardial valves. The key point about pericardial valves is that they are constructed—they are not harvested, God didn't make them—and as a result of that, every single pericardial valve is different. I don't believe you can group pericardial valves for follow-up, and I don't believe you can draw conclusions about pericardial valves in general. The conclusions must be type specific.

As far as the Ionescu-Shiley valve is concerned, we had cohorts of patients operated on between 1975 and 1980 with Starr ball valves, Hancock porcine valves, valve repairs of an extensive kind, and the Ionescu-Shiley bovine valve, all in the mitral position. There's absolutely no question about the inferior performance in the mitral position of the Ionescu-Shiley valve. The steep portion of the freedom from valve-related deterioration curve represents tears, the portion of the curve that is parallel with the Hancock valve represents calcification.

However, when we look at valve survival in the aortic position, the curves of freedom from valve-related death and valve-related deterioration for the bovine Ionescu-Shiley and the porcine Hancock valves are precisely the same. This same device made of the same material behaves completely differently in the aortic and the mitral position as Dr Pelletier pointed out, and the reason in this particular case is probably a very simple one. When you stretch pericardium across a large orifice it cannot stand the stress. When you stretch it across a small orifice the mode of failure becomes calcification as opposed to tearing.

I would just ask Dr Pelletier to confirm for this audience, please, that when you talk about pericardial valves you must talk about them specifically and not in general.

DR SHLOMO GABBAY (Newark, NJ): I congratulate Dr Pelletier for this excellent presentation. I was delighted as well to hear the last sentence about the Carpentier-Edwards pericardial valve, which in up to 6 years of follow-up shows excellent results. Pericardial valve obviously is not a generic name. Each known pericardial valve stands on its own merit due to the difference in design. We cannot blame the Carpentier-Edwards pericardial valve for the problem of the Ionescu-Shiley valve. The Björk-Shiley valve is a pyrolitic carbon valve as is the St. Jude valve, and surgeons do not think all pyrolitic carbon valves are the same.

I predicted the superior clinical behavior of the Carpentier-Edwards pericardial valve over the Ionescu-Shiley valve more than 5 years ago. I based my prediction on in vitro accelerated fatigue testing and closed observations of clinically explanted bioprostheses. Dr Pelletier's conclusions about the superiority of the Carpentier-Edwards pericardial valve can only enforce the claim that pericardial valves are not all alike, as well as stressing the importance of in vitro fatigue testing as an excellent tool for evaluating new designs.

Another example is the prediction made in the same study relative to the Hancock pericardial valve (Vascor). This valve performed so badly in vitro that I had strong doubts about whether it should have gone to clinical trials. Needless to say, the valve was explanted by the hundreds 1 to 3 years after implantation.

Even the Ionescu-Shiley valve, with some minor modifications, can be considered a very good valve. Thousands of patients have had this valve for more than 10 years and are still doing very well.

A good deal of understanding of the quality of pericardial tissue selected for cusp material is available today. Histological studies of clinical Ionescu-Shiley valves done in our laboratories show that of the three cusps of each valve, at least two cusps have substantial collagen degeneration before implantation. Rarely, two cusps of the same valve could be considered "good cusps" by the new standards. This technology was not available when these valves were made. We have good reason to believe that the quality of the tissue selected for cusp material is an important factor in the variability of durability of the same generic valve.

We have seen that the pericardial sac has many anatomical as well as histological variations. Pericardium might look adequate to the naked eye but not in the microscope.

With improvements in design as well as improved quality control of the biological material, and prolonged durability proven in a fatigue tester, pericardial valves can be made to last much longer than the present proven record. My belief is that the last chapter on pericardial valves has not been written yet.

DR PELLETIER: I thank the discussants for their nice comments.

Dr Reul, in regard to the choice of the various types of bioprostheses, I must stress that this was not a randomized study, and the choice of the prosthesis was left to the individual selection of each surgeon.

Enlargement of the aortic root was rarely performed in this series, and this is a technique that we don't use very readily. We'd rather use a smaller aortic prosthesis, and this is probably one of the factors that explain the shift from porcine to pericardial valves in latter years, with the hope that these bioprostheses would do better in the small aortic size.

In regard to the increased incidence of endocarditis in double-valve replacement with pericardial bioprostheses, I have no clear explanation for that observation other than that it may reflect the tendency in recent years for early operation in complicated cases of endocarditis, which include particularly prosthetic valve endocarditis and double-valve endocarditis.

As for the various types of pericardial prosthesis, you inquired about the number implanted in each group and whether a difference could be demonstrated. We have looked at that in a more detailed study which is actually going on, and the data that we've had so far indicate that indeed there are significant differences between Ionescu and Carpentier-Edwards valves, and that the numbers are sufficient to show such differences in valve survival, particularly in the mitral position. As for the Mitroflow prosthesis, it's a little more difficult to tell because the numbers are smaller, though actually it appears that in the mitral position, valve survival with the latter falls right in between the other two valves.

You questioned whether there remains an indication for the use of pericardial valves today. I think this is a matter of individual choice. Actually, there are no reasons for rejecting all pericardial valves. We have shown that some pericardial valves do not perform adequately in the mid-term and long-term range, but that others, such as the Carpentier-Edwards, appear to perform as well as the porcine valves, at least up to 6 years. So I think this remains an individual choice, although there is no clear advantage of one over the other.

Dr Frater, you stressed the point that the various pericardial valves are different, and I completely agree with you. This is clearly shown in our study, and our data support this conclusion. As major differences were found between porcine and pericardial valves, specific analysis of each type was necessary among the pericardial group, as shown in the last part of our data.

Dr Gabbay, I agree with you that the fate of the various prostheses could be predicted based on an analysis of the design of the valve, because I am convinced that early failure of the Ionescu-Shiley valve, at least in the mitral position, is related to technical features in its design that differ markedly from other pericardial valves, particularly the Carpentier-Edwards.

Esophageal Function in Patients With Reflux-Induced Strictures and Its Relevance to Surgical Treatment

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Esophageal function was evaluated in 53 patients with increasing severity of esophageal injury caused by gastroesophageal reflux disease (study 1), and the findings were applied to the treatment of 28 patients with reflux-induced strictures (study 2). Fifty asymptomatic volunteers served as controls for both studies. In study 1 there were 14 patients without reflux complications, 14 with esophagitis grade I to III, 13 with esophageal stricture, and 12 with Barrett's epithelium (6 of whom had a stricture). The prevalence of a mechanically defective sphincter increased with the progression of the esophageal injury; 50% in the patients without complications to 84% and 92% in those with stricture or Barrett's epithelium, respectively. Similarly, a decrease in amplitude of contractions in the distal esophagus was observed in patients with stricture and patients with Barrett's epithelium. In study 2, these findings were applied in the surgical management of 28 consecutive patients with a reflux-induced stricture. Preoperative motility studies were performed after patients were dilated to 60F. Control of reflux by a Nissen fundoplication gave excellent (86%) to good (14%) results in patients who had relief of dysphagia after dilation or adequate motility, or both. Four patients with both persistent dysphagia after dilation and inadequate motility underwent resection. Transmural fibrosis was observed in all specimens. The criteria presented are helpful in the selection of the optimal surgical procedure for the treatment of dilatable reflux-induced strictures.

(Ann Thorac Surg 1989;47:362–70)

In the wide spectrum of gastroesophageal reflux disease, the formation of a stricture, whether associated with a columnar-lined epithelium (Barrett's esophagus) or not, represents a serious complication, and is often a challenging problem for the physician. Studies [1, 2] have indicated that a reflux-induced esophageal stricture is associated with a profound loss of sphincter pressure that leads to increased acid exposure in the distal esophagus. In such patients, medical antireflux therapy and dilations are frequently ineffective, and surgical repair of the defective cardia is usually necessary [3]. However, the results of operation for reflux-induced strictures are not as good as those for uncomplicated reflux disease (75% versus 91%) [4, 5]. This has been explained by extensive periesophagitis and esophageal shortening, which can place the repair under excessive tension, or an unrecognized defective esophageal propulsion, or both [6].

The aim of the following two studies was to clarify the loss of esophageal function that occurs with complications of gastroesophageal reflux disease and then to apply these findings to the management of patients with reflux-induced strictures.

Material and Methods

The following methods were common to both studies.

Esophagoscopy

Endoscopic examinations were performed by one individual (T.R.D.), and the severity of esophagitis, when present, was classified as follows: grade I, mucosal erythema; grade II, linear erosions; grade III, increase in depth and width of the linear erosions (cobblestone esophagitis); and grade IV, the presence of an esophageal stricture [7]. Strictures were classified into three degrees of severity:

Grade I (mild): Diameter greater than or equal to 12 mm; a 36F endoscope passes easily.
Grade II (moderate): Diameter greater than 10 but less than 12 mm; a 36F endoscope passes with difficulty.
Grade III (severe): Diameter less than 10 mm; a 36F endoscope does not pass through.

Patients with histologically proven columnar-lined epithelium in the esophagus more than 3 cm above the cardia [8] were considered to have Barrett's esophagus.

Esophageal Manometry

Manometry was performed using a single catheter assembly consisting of five fluid-filled polyvinyl tubes bonded together in such a way that the five 0.8-mm lateral openings were placed 5 cm apart and radially oriented 120 degrees from each other. The recording catheter was

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continuously perfused with distilled water by means of a low-compliance pneumohydraulic capillary infusion pump (Arndorfer Medical Specialties, Greendale, WI) at a rate of 0.5 mL/min [9]. Each tube was connected to an external pressure transducer (Statham transducer; model P2306 Gould, Cleveland, OH) positioned at the midaxillary level.

Before each test, the pressure transducers were calibrated using a mercury-filled manometer so that a change of pressure of 1 mm Hg corresponded to 0.5 mm on the recording paper. The pressure waveforms generated were printed by a Gould ES 1000 16-channel recorder on paper running at a velocity of 5 mm/s. A belt pneumograph (Hewlett-Packard) was positioned around the chest to record respiratory excursions. A piezoelectric transducer was taped to the neck at the level of the cricoid cartilage to record pharyngeal swallows.

Manometry was performed in the fasting state. All medications were discontinued 24 hours before the test. The recording catheter was placed through an anesthetized nostril into the stomach, with the patient or volunteer (control) in the supine position, and withdrawn at 1-cm intervals every 20 seconds back into the esophagus.

Three manometric characteristics of the distal esophageal sphincter were measured: sphincter pressure, abdominal length, and overall length. The end-expiratory gastric baseline pressure was used as a zero reference for pressure measurement. A persistent rise in pressure exceeding 2 mm Hg above the gastric baseline marked the distal border of the sphincter. The proximal border was marked by the point where sphincter pressure dropped to end-inspiratory esophageal baseline pressure. Five measurements of the distance between these two points were averaged, and the average represented the overall length of the sphincter.

The point at which the end-inspiratory pressure changed from a positive to a negative deflection represented the respiratory inversion point. Five measurements of the distance between the respiratory inversion point and the distal border of the sphincter were averaged, and the average represented the abdominal length of the sphincter [10].

The amplitude of the sphincter was measured as the difference (in millimeters of mercury) between the gastric baseline and the pressure at the respiratory inversion point during the middle of the respiratory cycle. Five measurements of sphincter pressure were obtained and averaged to obviate the variation of pressures at each orifice resulting from the radial asymmetry of the sphincter [11]. Normal values for sphincter pressure, abdominal length, and overall length were obtained from 50 controls. The presence of a mechanically defective sphincter was defined by observing one or more of the following characteristics: a pressure of 6 mm Hg or less, an abdominal length of less than 1 cm, and an overall length of less than 2 cm [10].

When the manometric study of the lower esophageal sphincter was completed, the upper hole of the catheter was positioned 1 cm below the lower border of the upper esophageal sphincter. To adjust for the differences in esophageal length, the body was divided into five segments, each accounting for one fifth (20%) of the whole length. The five record channels corresponded to the five segments except when the esophagus was excessively shortened. The patient or volunteer was requested to perform ten dry followed by ten wet swallows (5 mL of water) at 30-second intervals.

The esophageal motility record was read by a computer under the supervision of a physician. The amplitude of contractions was measured in millimeters of mercury between the mean intraesophageal baseline pressure and the peak of the contraction wave. The mean pressure of ten contractions was calculated for each segment. When the amplitude of an esophageal contraction in a segment dropped to less than 10 mm Hg, it was considered a failure of contraction and was not used to calculate the mean contraction amplitude for that segment. When this occurred, the wave was classified as an interrupted wave. The duration of a contraction was expressed in seconds by measuring the time from the onset of the major upstroke of the contraction to the point at which the contraction returned to the esophageal baseline pressure. The velocity of propagation was expressed in centimeters per second and calculated by dividing the distance (in centimeters) between the recording sites by the time that elapsed (in seconds) between peaks of contractions in consecutive channels. When the velocity between the two peaks was 20 cm/s or more, the contractions were considered to be simultaneous. Normal values for amplitude, duration of contraction, and velocity of propagation were obtained from the 50 controls.

Esophageal pH Monitoring

Twenty-four hour pH monitoring of the distal esophagus was carried out using a glass electrode (Ingold, Copenhagen, Denmark) and a portable solid-state monitor (Synectics, Irving, TX), which sampled and stored esophageal pH at 4-second intervals. The probes were calibrated in a standard buffer solution at a pH of 7 and 1 before and after monitoring. The pH probe was then passed transnasally and positioned 5 cm above the upper border of the lower esophageal sphincter, as determined by prior manometry. The patient or volunteer was sent home and instructed to remain in the upright or sitting position until he or she retired for the evening, to avoid strenuous exertion, and to follow a diet sheet restricting him or her to three meals composed of food with a pH between 5 and 7. Only water was permitted between meals. A diary was kept of food and fluid intake, symptoms experienced during the monitoring period, the time when a supine position was assumed in preparation for sleep, and the time of rising in the morning. At the end of the test, the stored data were transferred to an IBM personal computer and analyzed using a commercial software program (Gastrosoft, Irving, TX).

A fall in pH to 4 or less was defined as acid reflux. The amount of esophageal acid exposure was scored using a previously published mathematical formula based on the mean value and standard deviation for six components of the 24-hour record: percentage of time the esophageal pH was 4 or less for the total 24-hour period; time in the upright position and the supine position; the total number

Table 1. Lower Esophageal Sphincter Manometric Characteristics[a]

		Patient Group			
Variable	Controls	No Complications	Esophagitis	Stricture	Barrett's Epithelium
Pressure (mm Hg)	14.8 ± 0.7	9.8 ± 1.8[b]	7.0 ± 1.9[b]	6.7 ± 1.2[b]	3.4 ± 0.6[b,c]
Abdominal length (cm)	2.2 ± 0.9	1.3 ± 0.8[b]	1.1 ± 0.1[b]	0.6 ± 0.2[b,d]	0.7 ± 0.1[b,d]
Overall length (cm)	3.6 ± 0.1	3.3 ± 0.3	2.8 ± 0.4[b]	2.2 ± 0.3[b,d]	2.02 ± 0.2[b,c]

[a] Data are shown as the mean ± the standard deviation. [b] Significance: $p < 0.001$ compared with controls. [c] Significance: $p < 0.005$ compared with patient group without complications. [d] Significance: $p < 0.05$ compared with patient group without complications.

of reflux episodes; the number of episodes lasting five minutes or longer; and the duration of the longest reflux episode expressed in minutes [12]. Patients whose cumulative score exceeded the mean score previously published [10] for controls by more than two standard deviations were considered to have an abnormal esophageal exposure to acid gastric juice.

Controls

Fifty asymptomatic volunteers without a history of foregut symptoms, upper gastrointestinal disease, or previous operation in the upper abdomen formed the control group for both study 1 and study 2. There were 19 men and 31 women with a median age of 35.8 years (range, 23 to 71 years). Each volunteer signed an informed consent form. All had esophageal manometry and 24-hour pH monitoring at Creighton University Surgical Gastrointestinal Diagnostic and Research Center.

Statistical Analysis

All values were expressed as mean and standard error. The Kruskal-Wallis and Mann-Whitney U test were used to compare the difference of the manometric characteristics of the lower esophageal sphincter and the components of 24-hour pH monitoring. Log and root square transformation was applied to the duration and amplitude of the esophageal contractions, and statistical difference between groups was tested using one-way analysis of variance and the Tukey test. The χ^2 test was used to compare proportions.

Study 1

This study was done to evaluate the loss of esophageal function that occurs with complications of gastroesophageal reflux disease.

Methods

Fifty-three symptomatic patients with abnormal acid exposure in the distal esophagus proven by 24-hour pH monitoring were entered into the study. Patients who had previous biliary, gastric, or esophageal operation, a primary esophageal motor disorder, or collagen diseases were excluded.

Patients were stratified into four groups according to the severity of esophageal injury on endoscopy: (1) 14 patients with uncomplicated gastroesophageal reflux disease, ie, absence of esophagitis (9 women and 5 men; median age, 59.3 years; range, 40 to 71 years); (2) 14 patients with grade I to III esophagitis (6 women and 8 men; median age, 49 years; range, 32 to 67 years); (3) 13 patients with an esophageal stricture classified as mild in 4, moderate in 6, and severe in 3 (2 women and 11 men; median age, 62 years; range, 50 to 78 years); and (4) 12 patients with Barrett's esophagus, 6 of whom had a stricture, which was graded mild in 1, moderate in 2, and severe in 3 (4 women and 8 men; median age, 53 years; range, 54 to 70 years). All patients had esophageal manometry and 24-hour esophageal pH monitoring at Creighton University. Moderate or severe strictures were dilated up to 60F a median of 11.5 days (range, one day to 60 days) before the performance of motility studies.

Results

The results of lower esophageal sphincter pressure, abdominal length, and overall length in the healthy volunteers and patients grouped according to the endoscopic findings are summarized in Table 1. There was a significant difference in sphincter pressure and abdominal length between the controls and all patient groups. A difference in the overall length of the sphincter was observed only between controls and patients with complicated reflux disease, ie, esophagitis, stricture, or Barrett's epithelium.

The patients showed a progressive deterioration of distal esophageal sphincter pressure, abdominal length, and overall length with increasing severity of esophageal injury. Patients with Barrett's esophagus had a significantly lower sphincter pressure than those with no complication. A shorter abdominal length and overall length of the sphincter were also observed in patients with stricture and patients with Barrett's epithelium compared with patients without a complication.

A progressive increase in the prevalence of a mechanically defective sphincter, as defined in the Material and Methods section, was associated with increasing esophageal injury (Fig 1).

Similarly, a progressive reduction in the amplitude of esophageal contractions was observed as the complications of reflux became more severe (Fig 2). Compared with controls, patients with stricture or Barrett's epithelium had significantly lower amplitudes of esophageal contractions in the distal three segments of the esophagus after dry and wet swallows. The duration of the contraction was not affected.

Patients with a stricture or Barrett's epithelium had a

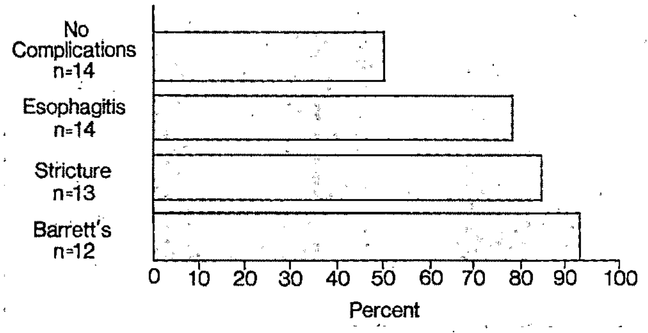

Fig 1. Prevalence of a mechanically defective cardia, defined as pressure of 6 mm Hg or less, abdominal length shorter than 1 cm, overall length shorter than 2 cm, or any combination of these, in patients with progressive severity of esophageal injury.

significantly higher prevalence of interrupted waves compared with the controls; the patients had an increased failure of contraction in the lower esophageal segments with severe esophageal injury. Patients also had progressively more simultaneous contractions associated with increasing injury of the esophagus, but the difference was not significant (Fig 3).

Figure 4 shows the acid exposure in the distal esophagus as measured by 24-hour pH monitoring. There was a progressive increase in esophageal exposure to gastric juice with increasing severity of esophageal injury. Patients with columnar-lined epithelium had a significantly greater acid exposure (expressed as percentage of total time, time upright, and time supine) compared with patients with uncomplicated reflux disease. These studies showed that a loss in function of the esophageal body and distal sphincter occurred in patients with severe injury to the esophagus and that this loss of function was associated with an increase in esophageal exposure to acid gastric juice.

Study 2

This study was done to evaluate the application of the results of study 1 to the surgical management of patients with reflux-induced esophageal strictures.

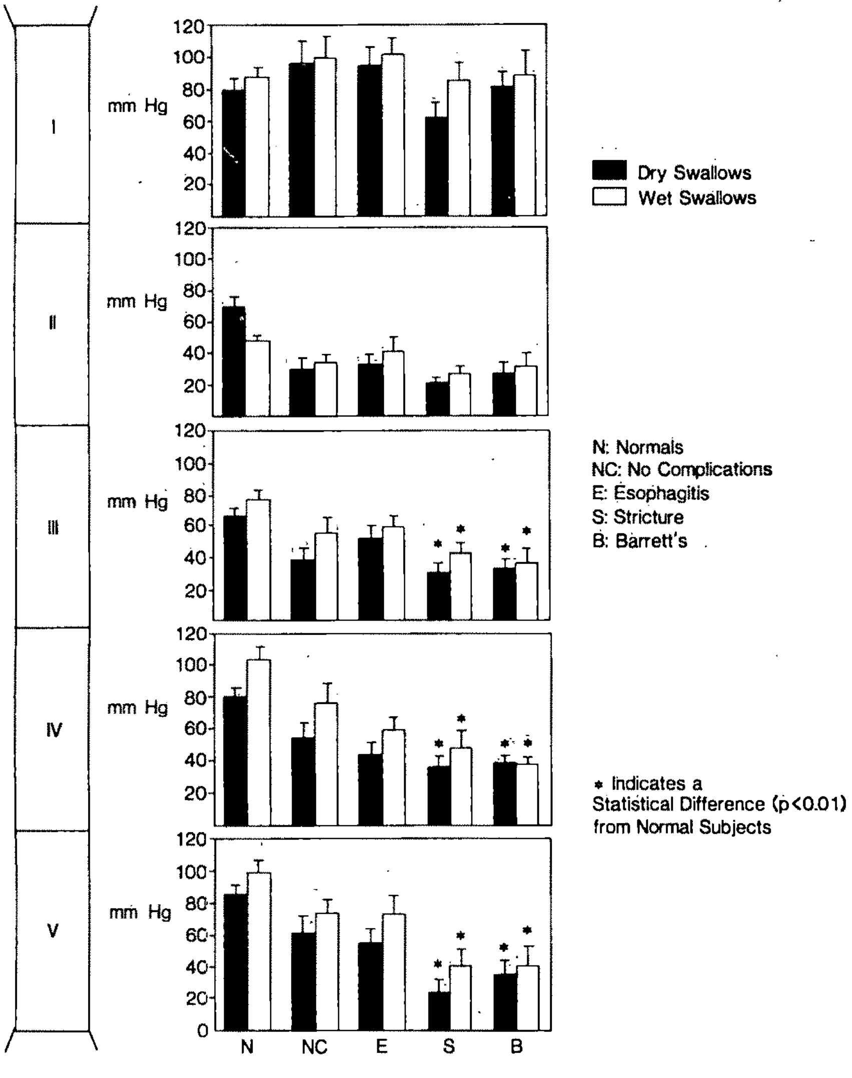

Fig 2. Amplitude of esophageal dry (solid bars) *and wet* (open bars) *contractions in controls and patient groups measured for each segment of the esophageal body. Patients with stricture* (S) *and patients with Barrett's epithelium* (B) *had a significantly lower amplitude in the lower three segments of the esophagus* (* = p < *0.01 versus controls).* (E = *patients with esophagitis;* N = *normal controls;* NC = *patients with no complications.)*

Methods

The study population consisted of 28 consecutive patients with esophageal strictures and abnormal acid exposure of the distal esophagus proven by 24-hour pH monitoring referred to one individual (T.R.D.) from 1978 to March 1988. Seventeen of these patients were seen at Creighton University Medical Center and 11, at the University of Chicago Medical Center (Chicago, IL). There were 19 male and 9 female patients with a median age of 59 years (range, 17 to 78 years). Patients with previous gastric or esophageal operation, primary motility disorders, or collagen-vascular disease were excluded.

Dysphagia was present in all 28 patients and was the predominant symptom in 22. Heartburn was the predominant symptom in 3, and substernal pain, choking, or asthma occurred in 1 patient each. Fifteen patients had had multiple dilations prior to referral. In all patients, the stricture was confirmed and classified according to the three degrees of severity by upper gastrointestinal endoscopy. Esophageal stricture was classified as mild in 4, moderate in 11, and severe in 13 patients. Barrett's epithelium was present in 7 patients.

Management consisted of progressive esophageal dilation using Maloney dilators of increasing diameter. All patients (except 1 with a mild stricture) were dilated to a maximum diameter of 60F before motility studies were performed. In 7 patients it was necessary to perform the first dilation under general anesthesia with fluoroscopic control using wire-guided Sippy dilators (V. Mueller, Chicago, IL). It was necessary for 10 patients to perform daily self-dilation using a 60F Maloney dilator to obtain an adequate assessment of the response to dilation. A good response to esophageal dilation was recorded if the patient reported that dysphagia was completely relieved. This occurred in 21 of the 28 patients. Esophageal motility studies were performed a median of 11.5 days (range, one day to 60 days) after dilation to 60F.

The motility studies performed before computerization of the method, ie, those done at the University of Chicago, were measured by hand by one of us (G.Z.), and the results were entered into the computer. The individual patient values and median values for sphincter pressure, abdominal length, and overall length are shown in Figure 5. A mechanically defective distal sphincter, as previously defined, was present in 23 of the 28 patients. Impaired motility of the esophageal body was defined as a mean amplitude of contractions lower than the 2.5 percentile of the controls or more than 50% of interrupted waves in one or more of the distal three segments. This was observed in 13 patients (Fig 6).

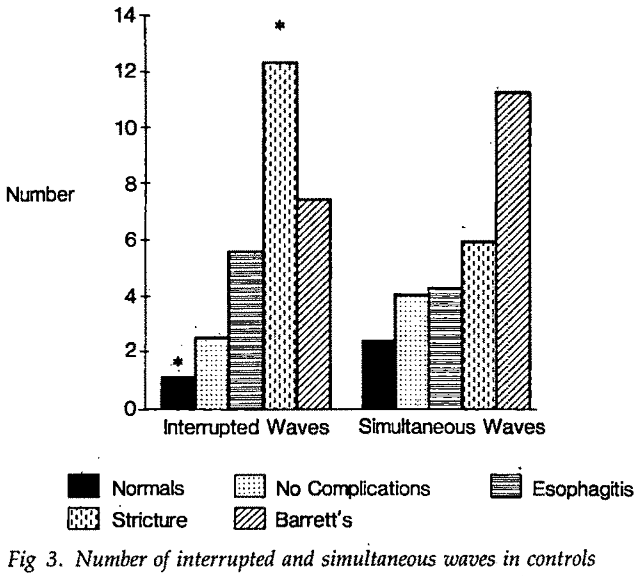

Fig 3. Number of interrupted and simultaneous waves in controls (normals) *and patient groups. Patients with stricture had a greater number of interrupted waves than controls (** = $p < 0.05$*).*

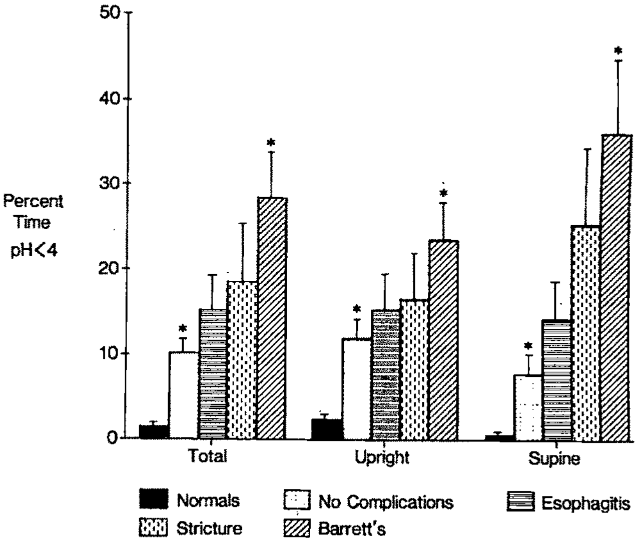

Fig 4. Acid exposure in the distal esophagus expressed as percentage of total time and time in the upright position and the supine position during which pH was less than 4 in controls (normals) *and patient groups. Results in all patient groups were significantly different from those in controls. Patients with Barrett's epithelium had a greater acid exposure than those with no complications (** = $p < 0.05$*).*

The selection of the operative procedure was based on the response to dilation and the result of the motility study (Table 2). The Nissen fundoplication was performed according to the technique previously described by our group [5]. The approach was transthoracic in 10 and transabdominal in 13 patients. In addition, a parietal cell vagotomy was performed in 3 patients and a cholecystectomy in 1 patient.

Esophageal resection and colon interposition was performed according to the technique previously described by our group [13]. Of the 5 patients who met the criteria for resection, 3 had inadequate motility in the lower three esophageal segments and 2, in the lowest segment. In 2 patients the resection was extended to the aortic arch; in 2 others, a total thoracic esophagectomy was done with the esophagocolic anastomosis performed in the neck. One patient with a severe stricture, who was a candidate for resection, underwent an antireflux procedure because of advanced chronic obstructive airway disease. In the 4 patients who had resection, the stricture was classified as mild in 1 and severe in 3. The resected specimens were histologically reviewed in an effort to relate morphological changes to the loss of esophageal function.

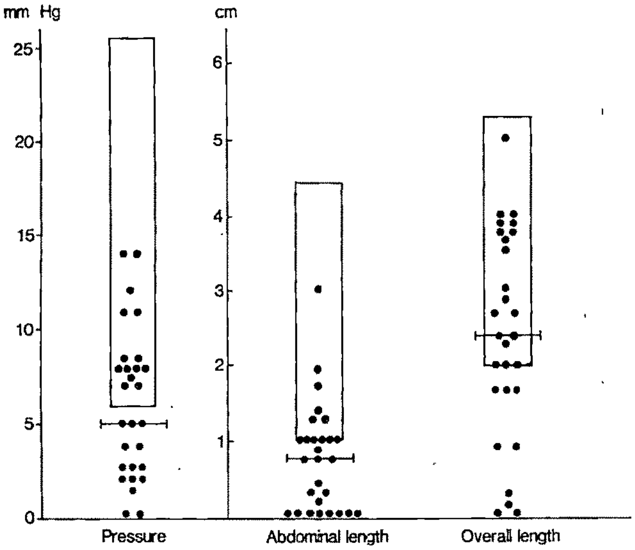

Fig 5. Individual distribution and median of lower esophageal sphincter pressure, abdominal length, and overall length in 28 consecutive patients with reflux-induced esophageal stricture. Shaded area represents normal range (2.5 to 97.5 percentile).

Postoperative evaluation consisted of an interview with the patient in the clinic or by telephone. A standard questionnaire was used to collect the data and assure completeness of the clinical evaluation. Questions were constructed to detect the symptoms of heartburn and regurgitation as indicators for the recurrence of reflux and the symptom of dysphagia as an indicator for the recurrence of a stricture or loss of esophageal function. The need for postoperative dilation was recorded. To avoid bias, dysphagia was defined as any discomfort in swallowing. The results of operation were graded as excellent if no symptoms of reflux or dysphagia were present, good if occasional dysphagia occurred (one episode per month or less), and poor if the patient complained of dysphagia more than once per month, had recurrent symptoms of reflux, or required dilations.

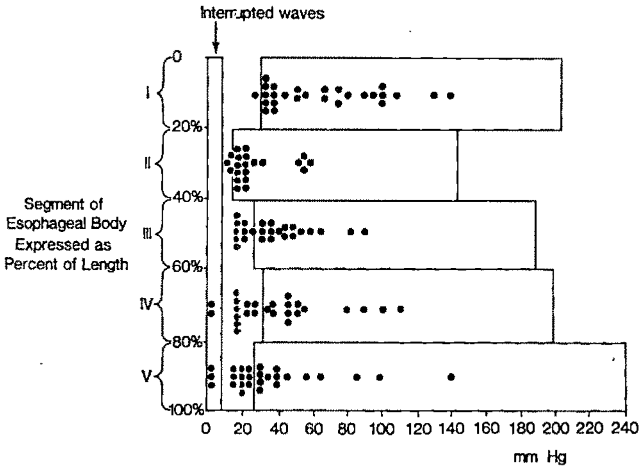

Fig 6. Individual distribution of amplitude of esophageal contractions in 28 consecutive patients with reflux-induced esophageal stricture. The shaded area represents the normal range (2.5 to 97.5 percentile) of amplitude for each segment of the esophageal body. In patients with short esophagi, only three or four segments were able to be measured.

Table 2. Selection of Operative Procedure in 28 Patients

No. of Patients	Response to Dilation	Esophageal Motility	Procedure
5	Poor	Impaired	Esophagectomy and colon interposition (one Nissen fundoplication[a])
2	Poor	Adequate	Nissen fundoplication
8	Good	Impaired	Nissen fundoplication
13	Good	Adequate	Nissen fundoplication

[a] Pulmonary function prohibited resection.

Results

A poor response to dilation was more common in patients with severe stricture (44%) than in those with moderate stricture (10%) ($p < 0.05$). Patients who had a poor response to dilation had a greater prevalence of impaired motility (71%) than those who had a good response (38%), but the difference was not significant. The prevalence of inadequate motility increased with the severity of the stricture as classified endoscopically, but this relationship was also not significant.

A median follow-up of 2.5 years (range, 6 months to 8 years) was obtained in 27 of the 28 patients after operation (Table 3). One patient was lost to follow-up. All patients were free from reflux symptoms. Only 1 patient had persistent dysphagia. This was the patient in whom an esophageal resection was indicated, but because of poor pulmonary function, an antireflux procedure was performed. The overall results for the other patients who underwent a Nissen fundoplication were excellent in 86% and good in 14%. No differences were observed in the results of operation between patients who had a good response to dilation and adequate esophageal motility and those who had a good response to dilation and impaired motility (86% versus 85%). Both patients who had a poor response to dilation but adequate motility also had an excellent result after a Nissen fundoplication.

The four resected specimens had mucosal ulcers in the region of the stricture. Three were lined by squamous epithelium and one, with Barrett's mucosa. In addition to ulceration and acute inflammation, chronic changes in the form of increased submucosal collagen and loss of muscle fibers were observed. Each resected specimen contained at least one area of transmural fibrosis (Fig 7).

Comment

Study 1 showed that the complications of gastroesophageal reflux are associated with an increased prevalence of a mechanically defective sphincter, progressive deterioration of esophageal contractility, and longer exposure of the esophageal mucosa to acid gastric juice. Of importance is the finding that 50% of patients without a complication of the disease have a mechanically defective sphincter. This suggests that the decrease in sphincter

Table 3. Results of Surgical Therapy for Reflux-Induced Strictures

Operation	No. of Patients	Symptoms of Gastroesophageal Reflux	Dysphagia			Postoperative Dilations
			None	1/Month	>1/Month	
Fundoplication	23[a]	0	19	3	1	0
Resection	4	0	4	0	0	0

[a] One patient was lost to follow-up.

function was not the result of inflammation or tissue damage; rather, these changes follow the loss of sphincter function.

If a stricture is observed in a patient with a mechanically normal sphincter and a normal 24-hour pH monitoring test, the likelihood is that it is secondary to a drug-induced injury. Treatment of such a patient consists of dilation only, as reflux is not an etiological factor [14].

On the other hand, simple dilation and medical therapy of a reflux-induced stricture is likely to fail because of the high prevalence of a mechanically defective sphincter in patients with complications of gastroesophageal reflux disease. Lieberman [3] has shown that patients with such a defect respond poorly to medical therapy and are prone to relapse. Alternatively, surgical therapy can stop reflux at this stage of the disease by correcting a mechanically defective cardia and reversing the pathophysiology that leads to stricture formation.

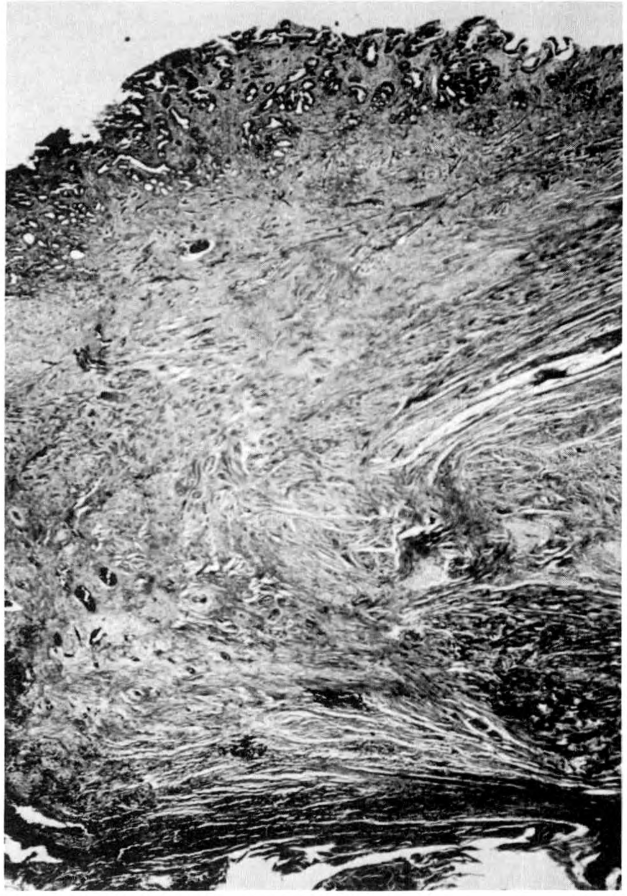

Fig 7. Cross section of esophageal wall. Note the glandular mucosa and the transmural fibrosis. (Masson's trichrome; ×33 before 32% reduction.)

However, successful surgical therapy is dependent on the remaining esophageal function. If scarring is of such severity that dilation is not possible, resection is required. Problems arise in patients who can be dilated to 60F but have inadequate esophageal body function to provide effective bolus propulsion after an antireflux procedure. These patients have persistent postoperative dysphagia and probably account for the reported 20% unsatisfactory results [15]. Identification of the patients in whom resection is a better alternative would improve the results of surgical therapy.

Study 1 demonstrated that the complication of a stricture is associated with a loss of esophageal contractility. Based on this observation, we used in study 2 the patient's response to dilation and the motility findings to select the surgical procedure. Accordingly, resection was performed in 4 patients who were able to be dilated to 60F but had persistent dysphagia and inadequate esophageal contraction. Histological examination confirmed full-thickness fibrosis of the esophageal wall. This would explain both the poor response to dilation and the loss of esophageal function. It is likely that dysphagia would have persisted in these patients if an antireflux operation had been performed. Indeed, the 1 patient who met the criteria for resection but had an antireflux procedure instead continued to experience postoperative dysphagia.

Patients who had a poor response to dilation but adequate motility and those with a good response to dilation but poor motility had similar good results after antireflux procedures. Presumably this occurred because adequate function was present despite a poor response to dilation, the function deficit was not as severe as measured, or the function deficit improved after the elimination of reflux [16]. Patients with a good response to dilation and adequate motility all had excellent results after an antireflux operation.

Application of the following three selection criteria should improve the results of surgical therapy for reflux-induced strictures by resecting the esophagus in those patients who are likely to have persistent postoperative dysphagia after simple dilation and antireflux repair.

1. Patients who have relief of dysphagia after dilation to 60F, independent of the motility findings, can be expected to have an excellent or good result from an antireflux procedure.
2. Patients who have adequate motility but poor relief of

dysphagia after dilation to 60F can be treated with an antireflux procedure with the expectation of a good result.
3. Patients who have inadequate motility and poor relief of dysphagia after dilation to 60F should be considered for resection.

In addition, our results suggest that, ideally, an operation should be performed before esophageal function is destroyed from continuous exposure to gastric juice through a mechanically defective sphincter or by repetitive dilations when a stricture is present.

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DISCUSSION

DR ROBERT J. GINSBERG (Toronto, Ontario, Canada): Dr Zaninotto and colleagues have elegantly demonstrated progressively deteriorating manometric changes in patients with increasing severity of endoscopic injury from reflux disease. However, one must be cautious when comparing a control group with a median age of 25 with a group of patients with a median age of 55.

All of us treating patients with dilatable reflux-induced strictures recognize that a certain proportion of surgically treated patients do not do well. We also recognize that severe strictures, primary motor disorders, and previous gastric or hiatal operations can adversely affect that surgical result. All of us would like to be able to predict accurately preoperatively those patients without the aforementioned problems that will fail to be improved by an antireflux procedure.

The authors have utilized manometry and symptomatic response to dilation as their predictors. Have they succeeded in this attempt? Theirs was not a prospective study, nor was it a retrospective analysis of all their failed antireflux procedures. The fact that the only patient with their criteria for surgical failure who had an antireflux procedure did indeed fail that procedure does not yet prove their point. Similarly, the fact that the 4 patients undergoing resection because of their criteria are improved in short-term follow-up does not prove long-term success. What is needed is a very long-term prospective study and, if available, a detailed analysis of all their previously failed antireflux procedures to confirm their hypothesis. Whether primary resection or the addition of a much more simple gastroplasty to a fundoplication is required to improve their success rate is a moot point.

The authors seem to suggest that the motility disorders identified are the cause rather than a secondary result of the reflux-induced esophageal injury. How can they then explain previous observations of improved motility after antireflux operations?

I congratulate the authors for the elegant study of manometric changes in reflux-induced esophageal injury. However, I do not believe that their indications for primary esophageal resection in dilatable reflux-induced strictures can be accepted without further detailed analysis of a larger group of patients, all followed for a minimum of 5 to 10 years.

DR DEMEESTER: We have just finished hearing the Michigan group report that 20% of patients who had a stricture continued to have dysphagia after dilation and an antireflux repair. The purpose of our paper was to try to identify those patients before operation.

There is no question amongst experienced esophageal surgeons that a patient with scleroderma and an esophageal stricture will have a poor result from dilation and an antireflux repair. This is due to the lack of contractility in the distal esophagus. It seems reasonable, therefore, that patients who have strictures and poor contractions in the distal esophagus would also have a high probability of a poor result after dilation and antireflux repair.

Based on this experience and reasoning, we prospectively compared the response to dilation and the adequacy of esophageal contraction on motility with the results of an antireflux procedure in patients with uncomplicated strictures; that is, no previous esophageal operation or motility evidence of scleroderma or diffuse spasm.

I focus your attention on the 21 patients who had an antireflux repair, that is, those who had a good response to dilation and good esophageal contractility in motility. All had an excellent to good result; that is, they did not require postoperative dilation and experienced no more than one episode of dysphagia per month. That's an extremely good result for a patient whose chief complaint preoperatively was persistent daily dysphagia that required repetitive dilation. This stands in contrast to a prevalence of postoperative dilations reported in other series. I would emphasize the severity of the stricture in the patients studied. In 13 patients the diameter of the lumen was 10 mm or less, and 7 of these patients required forceful dilation over a guidewire to open the stricture.

It is our opinion that patients who preoperatively had a poor response to dilation and inadequate esophageal contractility on motility study are better served by a resection, but, of course, that is open to debate. One may wish to try one's luck, but reason is on the side of resection. The patients who had a resection had the resected esophagus examined using staining techniques specific for fibrous tissue. All showed the muscle of the distal esophagus infiltrated with fibrous tissue, and in all the fibrosis extended through the full thickness of the esophageal wall. It is unreasonable to suggest that these patients would regain function after dilation and antireflux repair, particularly when their dysphagia did not improve with dilation preoperatively and their esophageal motility showed contractions less than 10 mm Hg in the distal portion of the esophagus. We therefore recommend the use of the criteria we presented as a means of selecting patients with a reflux-induced stricture who will, after dilation of their stricture and an antireflux procedure, be free of their problem.

In regards to our control population, the average age is 35, with a range of 23 to 71 years, and we are confident about the quality of the motility studies in these individuals.

Use of Silicone Stents in the Management of Airway Problems

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We report the use of a silicone rubber T tube for the management of complex airway problems in 47 patients during the past 15 years. The tube has been used for palliation in 11 patients with malignant obstruction of the airway, and as the sole treatment or as an adjunct to operation in 36 other patients. Based on the satisfactory results with the use of these tubes, we have utilized silicone stents in the bronchus and bifurcation prostheses at the carina. In the past, we have inserted the T tubes through a tracheostomy stoma. More recently, we have used a technique for endoscopic placement of the T tubes in which the horizontal limb is pulled out through the tracheostomy stoma. This technique facilitates introduction of the tube and maintains the airway during insertion. The use of silicone stents provides an important tool in the management of complicated airway problems, and we anticipate their increased use in the future.

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Over the past 15 years we have utilized silicone rubber prostheses for the management of complex airway problems in 53 patients. We [1] have reported our initial experience with the use of a tracheal T tube in 18 patients. Based on this early satisfactory experience, we have extended the use of silicone rubber prostheses in the airway, including bifurcation prostheses at the carina, and prostheses inserted into the main bronchi. The T tubes are manufactured by Hood Laboratories (Pembroke, MA), and come in a variety of sizes and lengths, and can be made to order for unique circumstances. Figure 1 demonstrates some of the currently available tubes.

Material and Methods

Between 1973 and 1988, 47 patients were treated with a tracheal T tube (including two T-Y tubes), 2 with a Y tube, and 3 with a bronchial stent. The T tubes were employed for benign disease in 36 patients and for malignant disease in 11 patients. For patients with benign disease, the T tubes served as definitive treatment, as a preoperative or postoperative adjunct to operation, or for management of an unsatisfactory result after operation.

Malignant Disease

Eleven patients with malignant tumors involving the airway were treated with T tubes. In 10 patients, the tube was used as definitive treatment to palliate obstruction or compression of the airway. In 1 patient, it was placed at the time of surgical resection of a subglottic tumor. In 2 of the 11 patients, the T-Y tube was utilized. This is a long silicone T tube with a bifurcation at the bottom end, which is situated at the carina.

Eight patients had squamous cell carcinoma involving the trachea or carina, 2 patients had involvement of the trachea from esophageal carcinoma, and 1 had compression by mediastinal lymphoma. The prostheses were in place from 2 weeks to 18 months (mean duration, 4.4 months). All patients have died of their disease.

In three instances, the T tube was removed and replaced with a tracheostomy tube, once after development of a malignant tracheoesophageal fistula, once because of the inability of the patient to keep the tube free from thick secretions, and once because of aspiration in a patient in whom the T tube extended above the vocal cords. Although the prosthesis is thin walled and easily compressed, compression of the tube by an enlarging tumor did not occur, although progression of the tumor beyond the end of the tube occurred in two instances.

Benign Lesions

The T tube was utilized for benign lesions in 36 patients: in 12 as definitive treatment; in 6 as a temporizing maneuver before resection; in 9 as an adjunct to operation; and in 9 for complications after tracheal resection.

DEFINITIVE TREATMENT. In 12 patients, the T tube was the sole treatment. Five patients had a postintubation stricture; 1, a caustic stricture of the trachea; 2, tracheomalacia after thyroid resection; 1, subglottic stricture secondary to relapsing polychondritis; and 1, stricture associated with Ehlers-Danlos syndrome. In the remaining 2 patients, the T tube served as a stent for a large tracheal defect secondary to prolonged tracheostomy. The upper limb of the T tube was positioned above the vocal cords in 5 patients and below the vocal cords in 7.

Extubation was successfully accomplished in 9 patients without subsequent difficulty after the prostheses had been in place for an average of 8.5 months (range, 1

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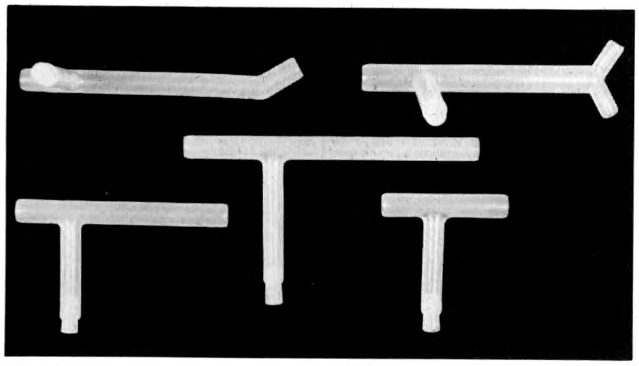

Fig 1. Silicone T *tubes in some of the available lengths. Each of the* T *tubes comes in various diameters. The tube in the upper left was specially designed for introduction into the left main bronchus (Illustrative Case Reports, patient 1). The tube in the upper right is the* T-Y *tube with a bifurcation at the carina.*

month to 12 months). In 1 patient with a complicated laryngeal and subglottic postintubation stricture, initial stenting with the T tube failed to resolve the problem. Laryngoplasty was performed with a good result. The tubes remain in place in 2 patients at 12 and 23 months. In these patients, the tracheal stricture is subglottic in location, and the upper end of the tube projects above the vocal cords.

PRIOR TO DEFINITIVE RESECTION. Six patients were treated with the T tube as a temporizing device prior to definitive resection. All 6 cases involved postintubation tracheal stenosis. Four of the patients had an associated illness or injury that prevented immediate repair; in the other 2, the T tube was used to allow active inflammatory mucosal changes to resolve before resection. The upper end of the T tube projected above the vocal cords in 2 patients and was below the vocal cords in 4. The average duration of intubation before resection was 10 months (range, 4 to 20 months).

ADJUNCT TO PRIMARY RESECTION. In 9 patients, the T tube was placed at the time of primary resection as an adjunct to the surgical repair. In all 9, the T tube was used to stent the immediate subglottic area and projected above the vocal cords. Three of the lesions were postintubation subglottic strictures, two were secondary to damage from irradiation, one involved a traumatic subglottic injury, one was caused by ingestion of a corrosive, one was due to tuberculosis, and one was a tumor (plasmacytoma) extending to the subglottic region.

Of the 8 patients, 1 subsequently required total laryngectomy for extensive irradiation damage to the glottic and supraglottic area. The T tube remains in place in 1 patient at 40 months. In the remaining 7 patients, the tube was removed after being in place 1 to 19 months (mean duration, 7 months). The long-term results were satisfactory.

FAILED PRIMARY REPAIR. In 9 patients, the T tube was used subsequent to surgical resection when the results of resection were unsatisfactory because of restenosis (6 patients), malacia (1 patient), or partial dehiscence (2 patients). In 4 of the patients the tube extended above the vocal cords.

One patient underwent subsequent re-resection for stricture with a good result. One patient with persistent tracheal malacia subsequently underwent surgical fixation of the membranous tracheal wall with a good result. One patient has the tube in place at 57 months. In the remaining 6 patients, the tubes were removed 3.5 to 19 months after insertion (mean duration, 8 months). One patient died at home three days after extubation; the cause of death was likely airway obstruction. Five patients had good airway function after extubation. One of these patients had repair of a traumatic tracheal disruption, required a T tube for partial anastomotic separation, and subsequently required tracheal resection 4 years after removal of the T tube.

Use of Silicone Stents Other Than T *Tubes*

As a result of airway complications that developed in several patients after single-lung and double-lung transplantation, we used a short segment of silicone tubing as a stent for the main bronchus in 2 patients and a Y-shaped prosthesis for stenosis of the distal trachea or proximal bronchus in 2 others. A bronchial stent was placed for a stricture due to tuberculosis in an additional 2 patients. These stents were all inserted endoscopically.

The initial bronchial stent was utilized for stenosis of the bronchial anastomosis after left lung transplantation. The stent has been in place for 3 years with no further difficulties. In the second patient, a bronchial stent was placed, also for an anastomotic stenosis, 2 months after left lung transplantation. Eleven months later, the stent was replaced with a slightly longer bronchial stent because of granulation tissue around the distal end. The stent has now been in place an additional 6 months without difficulties. Figure 2 shows the bronchial stent. Figure 3 is a computed tomographic scan of the stent in place in the left main bronchus.

A bronchial stent was placed in 1 patient for a chronic tuberculosis-caused stricture of the left main bronchus.

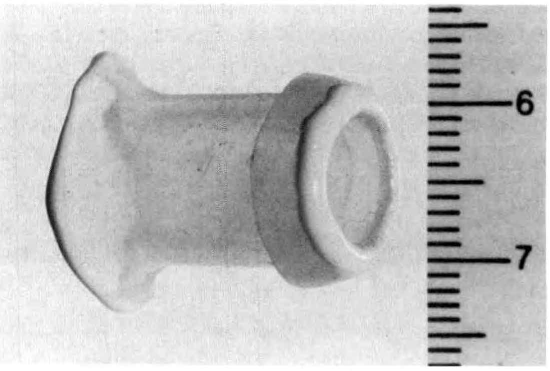

Fig 2. Bronchial stent fashioned from horizontal limb of silicone T *tube. The flared end, made from the junction of the horizontal and vertical limbs of a* T *tube, is placed distally. A small circle of silicone rubber is placed as a flange at the proximal end to prevent movement.*

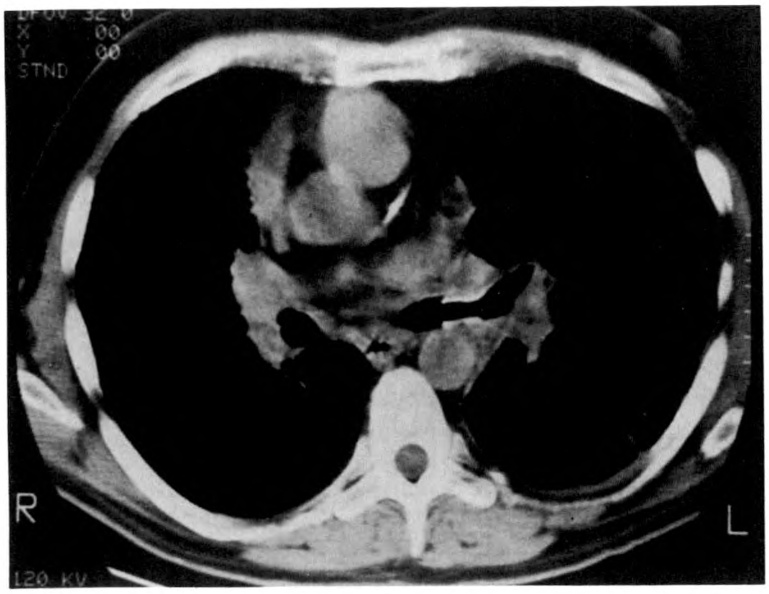

Fig 3. Computed tomographic scan demonstrating silicone stent in left main bronchus.

The bronchus was dilated, and the stent was endoscopically positioned. Two months later, however, the stent migrated proximally and was endoscopically removed; restenosis of the bronchus occurred. A similar stent was used in a 35-year-old woman with endobronchial tuberculosis, which had obliterated the left main bronchus and critically narrowed the right intermediate bronchus. The patient was seen in extremis. A stent was placed in the intermediate bronchus, and the patient did well for 3 weeks. However, she then was seen in severe distress at another hospital. The stent was deemed to have migrated and was removed; death occurred a short while later.

Eight of our initial 9 patients who had double-lung transplantation are alive and well [2]. A delayed stricture of the distal trachea and proximal bronchus developed in 2 of them, presumably as a result of ischemic injury. In each, a specially designed bifurcation stent was placed endoscopically (Fig 4). The stents have been in place for 12 months and 11 months. One patient has had no further difficulty. The second patient coughed up the initial stent several days after its placement. The stent was redesigned to have a greater angle between the two limbs. After placement of this new stent, the patient required bronchoscopy on two occasions to clear mucoid deposits from the stent.

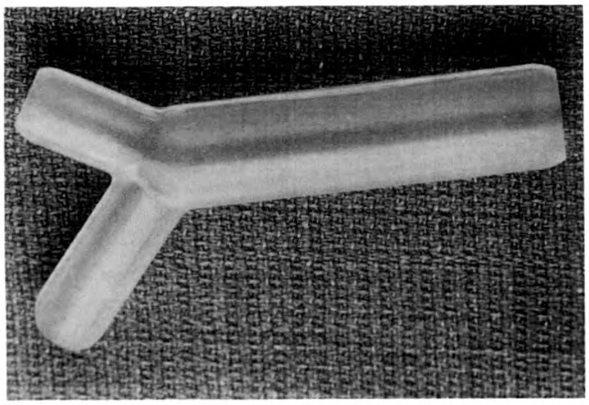

Fig 4. Y tube manufactured as stent for the distal trachea and proximal bronchi. The tracheal limb can be trimmed to a suitable length before endoscopic insertion.

Illustrative Case Reports

PATIENT 1. A 56-year-old man underwent right pneumonectomy for carcinoma of the lung at another institution in 1983. The postoperative course was complicated by development of a right bronchopleural fistula, which was treated initially by reexploration and stump closure and subsequently by repeat closure and thoracoplasty. The stump fistula reopened, and empyema ensued. A subsequent episode of respiratory failure was treated with mechanical support using a left endobronchial double-lumen tube. The patient recovered, but a distal tracheal stricture developed at the site of the tracheal cuff of the double-lumen tube.

Repeated dilations failed to maintain airway patency for any substantial time, and the patient underwent tracheal resection through a median sternotomy. At the time of resection, the right bronchial stump was reamputated at the level of the carina. The trachea was considerably ossified, and the carina was fixed by the previous procedures, thereby permitting only limited mobilization of the airway following resection. Furthermore, the blood supply to the carina was deemed in jeopardy because of the previous pneumonectomy and the necessary subcarinal dissection. For this reason, a vascularized pedicle of omentum was elevated from the abdomen and wrapped around the anastomosis.

Ten days after operation, the patient was clinically well and ready for discharge. Elective endoscopy, however, revealed partial disruption of the anastomosis, ischemic changes at the carina, and visible omentum. In spite of this, no clinical complications developed. Over the ensuing 2 months, the patient required repeated rigid bronchoscopy for dilation and debridement of the airway. A

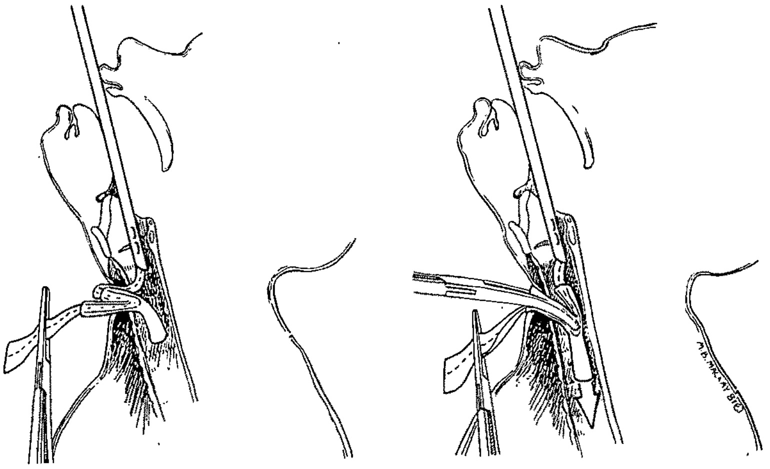

Fig 5. Technique of T *tube insertion through tracheostomy stoma. The distal end of the* T *tube is inserted through the stoma and directed toward the carina. It is then advanced distally until almost the entire tube is within the trachea. The lower end of the umbilical tape is held firmly while the upper end of the tape is pulled upward through the bronchoscope to advance the tube into proper position. (Reproduced from [1] by permission of The C.V. Mosby Company, St. Louis, MO.)*

long-limbed T tube was then inserted with its distal end in the proximal left main bronchus. This remained in place for 10 months. On its removal, there were persistent granular changes in the airway and subsequent redevelopment of stenosis. A special long-limbed T tube with an angled extension for the left main bronchus was obtained (see Fig 1) and inserted in October 1984. This type of tube has now been in place for an additional 47 months, with one change because of fraying of the end of the horizontal limb. The patient remains active without symptoms.

PATIENT 2. A 48-year-old woman had hoarseness and stridor, and was found to have subglottic laryngeal stenosis in 1983. On open biopsy of the larynx, a diagnosis of relapsing polychondritis was made, and a tracheostomy tube was inserted. Over the ensuing year, the patient lost her voice completely.

The patient was first seen by our service in June 1987 with a tracheostomy tube in place. She used a pharyngeal vibrator for speech. With considerable difficulty, a passage was created through the larynx down to the level of the tracheostomy tube using rigid bronchoscopy and dilators. A long-limbed T tube was positioned through the larynx in such a way that it projected above the vocal cords.

The patient's hospital course was complicated by the development of subcutaneous emphysema and cellulitis in the neck with formation of a localized abscess anterior to the larynx requiring drainage under local anesthesia. It was presumed that the previous laryngofissure had been fractured at the time of dilation. The inflammatory process resolved after drainage.

The patient had difficulty with aspiration of liquids for several weeks but ultimately regained the ability to swallow adequately and was able to speak with a soft but clearly understandable voice. Over the ensuing year, one episode of aspiration pneumonia occurred and necessitated hospitalization for a week. The T tube was removed and replaced 1 year after insertion for cleaning purposes.

Techniques of Insertion

We [1] have previously described a method for inserting the T tube through an existing or a newly created tracheal stoma. With this technique, the distal limb of the T tube is advanced through the stoma and into the airway as far as possible toward the carina. The entire tube, including most of the horizontal limb, is advanced distally until the upper limb can be folded on itself and pushed through the stoma into the trachea. An umbilical tape previously inserted through the mouth, out the stoma, and into the upper limb of the T tube is used to assist the process. When the upper end of the tube has been pushed into the trachea, traction on the umbilical tape from above helps pull the upper limb into place. Figure 5 depicts this technique.

More recently, we have often used a technique for placing the T tubes endoscopically through the larynx, as suggested by Duvall and Bauer [3]. A special no. 5 bronchoscope (Piling Surgical, Fort Washington, PA) has been constructed with an inflatable balloon at its distal end (Fig 6). The bronchoscope is inserted through the T tube and the cuff inflated to fix the tube to the bronchoscope. The well-lubricated prosthesis is then introduced through the vocal cords and advanced into the airway. A heavy silk ligature is passed into the tracheal stoma, withdrawn out the larynx, and tied to the end of the horizontal limb of the T tube before its insertion. After the T tube has been advanced into the trachea, traction on the silk suture helps deliver the horizontal limb through the stoma. The balloon at the end of the bronchoscope is then deflated, and the bronchoscope is withdrawn.

This method of insertion has the distinct advantage of maintaining constant control of the airway, so that the patient can be continuously ventilated with a Venturi tube as the T tube is being inserted and positioned in place. Furthermore, insertion of long-limbed tubes through a tracheostomy stoma has often proved difficult because the tube kinks and folds like an accordion as it is pushed into the airway. With the T tube mounted over the rigid bronchoscope and inserted from above, this no longer poses a problem. Insertion of a T tube for subglottic stricture has also been facilitated by the endoscopic method of insertion, as withdrawing the upper end of a T tube through a subglottic narrowing after insertion of the tube through a tracheostomy stoma can be difficult. After insertion, the horizontal limb of the T tube is frequently

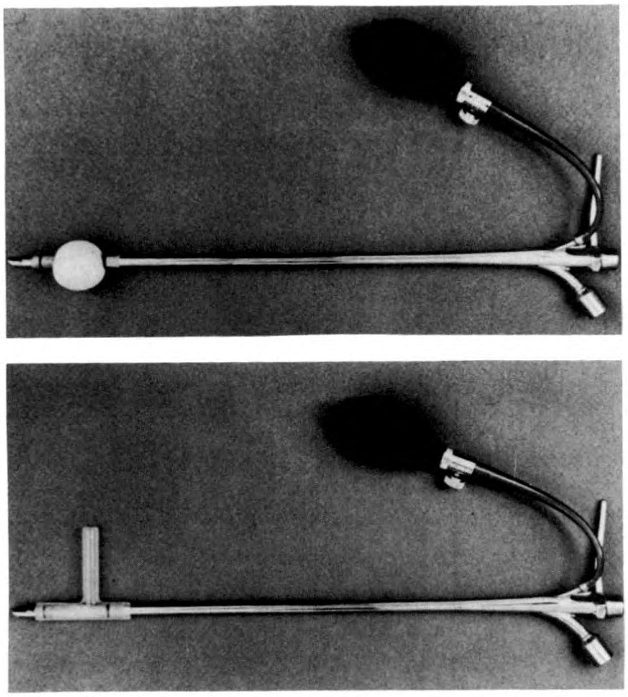

Fig 6. Special bronchoscope designed for peroral insertion of T *tube. The bronchoscope has an inflatable balloon at its distal end. The* T *tube is inserted over the bronchoscope, and the balloon is inflated to fix the* T *tube to the bronchoscope to facilitate insertion. A length of heavy silk is passed through the tracheal stoma and brought out through the mouth to be tied to the tip of the horizontal limb. The* T *tube and bronchoscope are inserted through the larynx, and the silk is used to facilitate extraction of the horizontal limb through the stoma.*

left uncorked overnight and the upper airway tested the following day by corking the horizontal limb to ensure that the airway is adequate.

Endoscopic insertion of the T tube can be performed without the special bronchoscope. Using a no. 5 rigid bronchoscope, an 8.5-mm endotracheal tube is inserted as a sheath over the proximal portion of the bronchoscope, leaving the distal portion of the bronchoscope unsheathed for a length sufficient to accommodate the length of the T tube to be inserted. The endotracheal sheath prevents the T tube from riding up on the bronchoscope as it is inserted. When the T tube is in proper position, the sheath is held in place while the bronchoscope is gradually rotated and withdrawn. The sheath keeps the T tube from being withdrawn along with the bronchoscope. This is the technique that has also been utilized for insertion of bronchial stents (Fig 7). To place the bifurcation stent, the sheathed bronchoscope is inserted through the tracheal limb to the tip of the left bronchial limb. The shorter right bronchial limb is guided into place by means of a Fogarty catheter previously put through the prosthesis, out the right bronchial limb, down the airway, and into the right main bronchus; proper placement is confirmed endoscopically.

Comment

The silicone T tube was developed and described in 1968 by Dr William Montgomery [4] for stenting the airway after repair of stenosis in the low subglottic region. It has subsequently been used for a variety of compressive and malacic lesions, and has been found to provide a safe, relatively trouble-free airway. As an alternative to tracheostomy, the T tube is nonirritating, provides respiration through the nasopharynx, thereby preserving humidification and speech, and in general requires little if any special maintenance or cleaning. When it has been necessary to stent the subglottic region, we have elected to have the upper end of the tube project just above the vocal cords to avoid injury to the cords from the top of the tube. In this series, 24 tubes protruded above the vocal cords. In these patients, subsequent extubation was not associated with vocal cord dysfunction, even after the tube had been in place for a year or more.

Although use of the T tube is not recommended as the primary treatment of tracheal stenosis, it has proved very useful in the management of complex airway problems as an adjunct to operation and occasionally as the sole treatment. In patients with unresectable primary or secondary tumor causing obstruction or compression of the trachea, a satisfactory airway can be provided by the T tube. This is especially appropriate when the patient has received maximum radiotherapy or has a tumor that has not responded to irradiation.

Our favorable experience with use of the T tube in the trachea led us to consider use of a silicone prosthesis for bronchial stenosis. In these patients, we have utilized twice-daily inhalation therapy with Mucomyst (acetylcysteine) to prevent buildup of tenacious secretions on the prosthesis. It is remarkable that the bronchial stent has been in place for up to 3 years without any complications in an immunosuppressed patient after lung transplantation.

When subsequently faced with the need to stent the carinal region because of stenosis after a double-lung transplantation, we thought that a small bifurcation pros-

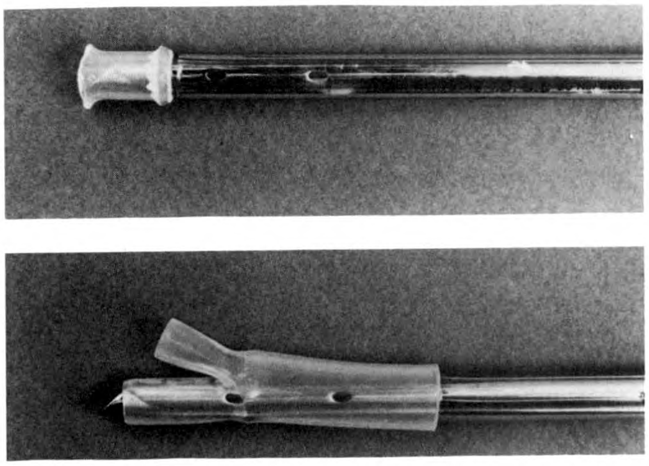

Fig 7. Technique for endoscopic insertion of bronchial stent and bifurcation stent. An endotracheal tube is placed over the bronchoscope as a "pusher" with the stent put over the tip of the bronchoscope distal to the pusher. When the stent is in place, the space between the endotracheal tube and bronchoscope is flooded with saline solution, and the bronchoscope is withdrawn while the pusher holds the stent in place.

thesis without a horizontal limb extending through a tracheostomy stoma might be satisfactory. The shape of the tube itself holds it in place. In this situation, we have also recommended use of Mucomyst inhalations twice daily. We have not performed routine flexible bronchoscopy on patients with indwelling stents, but the use of flexible bronchoscopy every 4 to 6 months might be advisable to confirm the absence of granulation tissue at the ends of the prosthesis and to cleanse the inside of the prosthesis using a small brush passed through the channel of the bronchoscope.

Because the silicone tube is so well tolerated in the trachea and the need to uncork the horizontal limb so rare, at least two reports [5, 6] have described shortening the horizontal limb and burying it subcutaneously with primary closure of the skin. This has proved problem-free for periods longer than 5 years.

In an early report, Montgomery [7] outlined in detail the care of the patient with a tracheal T tube, including suction through the horizontal limb twice daily and instillation of acetylcysteine three times daily. We have not recommended these methods because the patient's ability to cough and clear secretions from the T tube into the pharynx is normally satisfactory. This assumes that the horizontal limb of the tube will be kept plugged, as the upper limb can become obstructed if the horizontal limb is left open, thereby diverting the air flow from the upper limb. It is apparent that the silicone prostheses can be left in place for years without major complication.

When the T tube is used to stent an area of tracheal stricture in anticipation of subsequent extubation, it should remain in place, in general, at least 9 months, preferably longer, before extubation is attempted. When the T tube is used to stent an area of subglottic damage, a protective tracheostomy tube should be placed through the tracheal stoma at the time the T tube is removed to maintain a safe airway in case recurrent narrowing of the damaged area occurs. This can take several weeks to develop, and during this waiting period a fenestrated tube or a small corked, uncuffed tracheostomy tube can be used to temporarily preserve the tracheal stoma.

Our limited experience with the use of a bronchial or carinal stent suggests that the use of such stents can be extended to other conditions including malignancies. In 1987, Orlowski [8] reported the use of a bronchial stent in 7 patients because of a neoplasm.

The use of the silicone stent adds flexibility to the management of complicated airway problems, and we anticipate increased use of such stents in the future.

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DISCUSSION

DR HERMES C. GRILLO (Boston, MA): After this very thorough presentation, I can only add a few marginal notes about the use of the T tube by the thoracic surgeon. I think not enough thoracic surgeons are familiar with the T tube. I cannot tell you how many patients with basically unreconstructable tracheas for one reason or another have been sent to my colleagues and me. They arrived in Boston with tracheostomy tubes, which had made them miserable for years, and when they left, with a T tube in place, they could talk, breathe, and do everything but dive into a swimming pool. In fact, we have had a couple of patients who did that, although I would not advise it.

The earliest reference to T tubes that I have been able to find was in 1891 by a British surgeon reporting in *The Lancet*. He devised a metal T tube that was the exact configuration of the T tubes you have seen except it was transversely halved and had a collar over the side arm. Bill Montgomery's first T tube was a rigid plastic tube with a similar collar. Dr Montgomery, who works at the Massachusetts Eye and Ear Infirmary, devised a very useful silicone tube. There are many versions of it now all over the world.

It is a little ironical that the T tube was invented by Dr Montgomery chiefly for the definitive treatment of tracheal stenosis. The idea was that it would be left in place for 3 or 4 or 6 months, and then when it was pulled out, the stenosis would be cured. Tissues respond that way only in cases of partial-thickness stricture, and, as Dr Cooper pointed out, in such patients a good airway can be achieved without further surgical intervention. But in most patients, the definitive treatment of stenosis is surgical. If the T tube remains in a trachea for 5 years in the case of a full-thickness stricture, the lumen will just narrow again.

We have found the T tube useful at Massachusetts General Hospital for precisely the three indications described by Dr Cooper: first, for definitive treatment of either irreparable stenosis or palliation of tumors that have already been treated by every other method—coring out, laser vaporization, irradiation—and are at a point of extrinsic compression; second, to temporize when the patient's airway is too inflamed, as in the case of a tracheal burn, or when definitive surgical intervention should be deferred to a more favorable time; and third, for failed operations. Not every tracheal operation is successful; I can attest to that. The tube helps us out of the difficult situations and permits us to try again, if that is possible.

We differ from Dr Cooper in a minor respect. When we repair strictures that involve the subglottic larynx as well as the upper trachea, we do not see a need for splinting the anastomosis. Occasionally we do have a stoma below until the edema goes away, but the anastomosis itself can ride on its own.

I should point out that if a stent is maintained in a patient for a long period, when that patient returns to the hospital for possible resection, it is a good idea to pull the tube out 24 to 48 hours ahead of time so that the inflammation can subside. There is always inflammation, even around an inert substance like silicone. Also, this gives the trachea a chance to declare itself and allows the injured segment to start contracting.

I have a couple of miscellaneous comments that might be of some interest. Bill Montgomery has advised against cutting these tubes. Actually, based on the many peculiar cases that we see, it may be necessary to trim them to fit precisely, even though they come in a variety of lengths and sizes. We do this very simply with a scalpel, then bevel the edge with scissors and file the edge with sterile sandpaper in the operating room. If the tube doesn't fit correctly, we pull it out again, take off another 1 or 2 mm and put it back again; we repeat this procedure until the fit is just right. We have never seen any trouble with irritation from these sanded edges.

We also asked the Hood Company to make extra long tubes, which can be trimmed to fit unusual situations. If you need a tube for the left main bronchus, for example, in a patient who has a postpneumonectomy syndrome that has not responded promptly to mediastinal repositioning but still has severe malacia, there is not time to ask the company to make a specific tube that fits that patient's configuration. We found it useful to take a Hood salivary tube, which is used as an intraluminal esophageal stent, trim it down as I described, take the next size up of T tube, side arm, and collar, and fit that with a little silicone cement. The tube fits exactly as we want it.

I take heart from Dr Cooper's description of his internal stents and his T-Y tube use. We have placed a few T-Y tubes, both in adults and in children, and a number of these extra long tubes, and I have seen granulations occasionally where the tube fits rather snugly in the bronchus. We have been a little wary of those, but this has not been a major problem in Dr Cooper's experience.

Dr Cooper and colleagues have done a great service in presenting their extensive experience to this group. I encourage you to look into the use of these tubes. There are some tricks in their use, but they are extremely serviceable.

DR WILLIAM E. NEVILLE (Newark, NJ): After the superb paper by Dr Cooper and the discussion by Dr Grillo, his former mentor, I really do not have much to say except to give you some of the data that we have accrued over the years regarding our permanent intratracheal silicone prosthesis. Originally we obtained the prosthesis from Dow Corning and used it to replace the trachea and both stem bronchi. After 3 years of evaluation in dogs, we presented our data at the third annual meeting of this Society in 1967. There is no question that we need a tracheal prosthesis. We have the artificial kidney, we have heart valves, and we have artificial limbs, or else I would not be up here today.

I think the most important aspect of Dr Cooper's paper is that silicone has many attributes in an area where everyone originally thought that infection would occur, pulmonary secretions could not be eliminated, and disruption was inevitable. I have tried to stress over the years that this is not true. What I will tell you correlates with what Dr Cooper has presented with the exception that our prosthesis is designed and used as a permanent implant. During the past 20 years, we have used our prostheses in 25 patients with a variety of conditions—recurrent stricture, malignancy, tracheal malacia, and postirradiation tracheal stenosis. Seventeen had benign disease and 8, malignant.

We have utilized a long prosthesis in several patients by simply invaginating one prosthesis into another. One patient entered our hospital several months after a severe crush injury to the chest. He had a long stricture of the trachea, and we placed two prostheses through the tracheostomy. This can be done easily either through the existing tracheostomy or by making an incision in the neck.

Another patient, a woman with a long history of asthma and emphysema, had a respiratory arrest in Rome. She was transferred to the United States breathing on a respirator. She had two strictures and a tracheoesophageal fistula. We were unable to do a primary anastomosis. Consequently I placed a straight prosthesis into the trachea and sutured the opening in the esophagus. She has done very well in the past 10 years.

We have also utilized the prosthesis in patients with nonresectable cancer and patients with recurrent cancer in the trachea and at the carina. I think it certainly has a place in thoracic surgery and can be used by all of you who are interested in treating patients with a tracheal defect of such a magnitude that a primary anastomosis is impossible.

DR COOPER: Thank you very much, Dr Grillo and Dr Neville. As I learned so much of this subject from Dr Grillo, I am not in a position to disagree. Quite the contrary, I am in complete agreement with his comments.

I emphasize that for primary resection of the trachea in the subglottic region, stenting is not ordinarily required. However, in some patients, a small protective tracheostomy below the subglottic anastomosis might be placed for a few days. Our illustrative case reports were exceptions, not the rule.

To amplify another point, Dr Grillo mentioned that whenever one of these tubes is removed, it is always important to protect the airway for a little while because it can subsequently narrow again. Just because there is a good airway at 24 hours after tube removal does not mean that the airway will not narrow over the following week. I think your suggestion of use of the T tube in pediatric patients is also extremely interesting.

Dr Neville has presented over the years interesting experience with his prosthesis, and we have had points of agreement and points of disagreement. I think the major point of disagreement may be the use of a prosthesis for major resections of the airway. It has been demonstrated by Dr Grillo, Dr Pearson, and others that tracheal replacement is rarely necessary with the modern techniques of mobilization and resection. The use of a prosthesis as a replacement after a major resection clearly has a restricted use.

On the other hand, Dr Neville, maybe we have not been listening closely enough to the other aspect of what you have been presenting, namely, the valuable properties of silicone rubber. Over the years, we have thought a porous prosthesis or something else would be better. It is remarkable, though, how well tolerated the silicone rubber is. That is, of course, the common link between our use of the silicone stent and your use of the silicone prosthesis.

Of the 25 patients you referred to, 17 had benign disease and 8, malignant. Why not just insert a tube within the airway, rather than embark on a major resection, because then you have the second problem of wound healing and attachment of the trachea to the collar of the prosthesis and other problems, such as erosion of the innominate artery? I think we would enthusiastically endorse the properties of silicone rubber, as you have, as a conduit in the airway, but would recommend that it be used, as such, by an insertion technique. Also, of course, if it is inserted, it can later be replaced if necessary.

Dr Grillo reminded me on my way up to the podium of an interesting experience of both Dr Keszler and Dr Maeda. They have found the T tube is so well tolerated that they have cut off the horizontal limb and buried it beneath the skin in several patients; the tube has been in place this way for up to 5 years. I guess it eliminates the need for the gold chain and the safety pin, and it also has a nice cosmetic appearance.

Finally, we have been a bit surprised how well these stents are tolerated. This includes a long tube into the bronchus of the only lung in 1 patient, and a bronchial stent in an immunosuppressed patient. Both have been in place for up to 3 years without problems. The finding defies conventional wisdom, but this has been an interesting experience.

REVIEW OF RECENT BOOKS

International Trends in General Thoracic Surgery, Vol 4. Esophageal Cancer

Edited by Norman C. Delarue, Earle W. Wilkins, Jr, and John Wong
St. Louis, The C.V. Mosby Co, 1988
456 pp, illustrated

Reviewed by Douglas J. Mathisen, MD

The first three volumes of *International Trends in General Thoracic Surgery* have been an excellent addition to the surgeon's library, and volume 4 is no exception. The editors state in the foreword that "this forum will most effectively convey new information in relation to the practical aspects of actual patient care as well as emphasize the clinical application of the material." This goal is certainly accomplished in this volume.

The editors have solicited a truly outstanding group of international experts. Each chapter is very authoritative and well referenced. Many different viewpoints are presented and no attempt is made to bias the reader to one point of view or another.

Duranceau presents a comprehensive review of the etiological factors associated with esophageal cancer and regional differences around the world. Valuable information regarding techniques for staining with toluidine blue and Lugol's solution and cytologic screening for early carcinoma are presented in section 2. The difficult challenge of staging is presented in section 3, with helpful information about correlation of computed tomographic findings and operative findings. The role of endoscopic ultrasound in staging is also discussed.

The editors have recognized the high operative mortality often associated with esophagectomy and have devoted an entire section to methods of reducing perioperative mortality. Surgical technique and approach is closely tied into this concept and thoroughly covered by many leading authorities in sections 6 and 7. Two valuable contributions are Boretti's median sternotomy approach for upper thoracic and cervical cancers and Nanson's combined team approach.

Chapter 9 presents an up-to-date review of the multimodality approach to esophageal cancer. The contributors to this important section are recognized leaders in this area and present a thorough review of their experience.

John Wong states in chapter 21 that "surgeons must possess a repertoire of procedures that could be employed for tumors at various locations and of different stages." This book will expand the repertoire of all physicians dealing with esophageal cancer and will be a valuable addition to their personal library.

Boston, Massachusetts

Effect of Sodium Nitroprusside on Spinal Cord Perfusion and Paraplegia During Aortic Cross-Clamping

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To evaluate the effects of sodium nitroprusside (SNP) on hemodynamics, cerebrospinal fluid dynamics, and neurological outcome after 30 minutes of thoracic aortic occlusion, we monitored proximal and distal blood pressure, cerebrospinal fluid pressure, spinal cord blood flow, and somatosensory evoked potentials. In group 1 (n = 6), no attempts were made to control proximal hypertension, whereas in group 2 (n = 6), proximal blood pressure was controlled with intravenous infusion of SNP. There was no significant difference in proximal or distal blood pressure or cerebrospinal fluid pressure between the two groups at baseline. During the cross-clamp interval, the mean proximal aortic pressure rose from 108 ± 21 to 146 ± 14 mm Hg ($p < 0.001$) in the control group, whereas the mean blood pressure in the SNP group was maintained at 99.8 ± 12 mm Hg (p = not significant compared with baseline blood pressure). Mean distal aortic pressure decreased from systemic values to 23 ± 7 mm Hg in control animals and to 11 ± 5 mm Hg in the SNP group ($p < 0.005$). In the latter group, cerebrospinal fluid pressure increased significantly from 10.6 ± 1.9 to 20.1 ± 5.5 mm Hg ($p < 0.005$). In animals receiving SNP, spinal cord blood flow was decreased in the lower spinal cord segments and increased in the upper cord segments. When compared with controls, this difference did not reach significance. The use of SNP was associated with an earlier loss of somatosensory evoked potentials (3 minutes 32 seconds versus 11 minutes 1 second). All animals in the SNP group had negative spinal cord perfusion pressure (−9.9 ± 6.8 mm Hg) and sustained spastic paraplegia, whereas control animals with positive spinal cord perfusion pressure (+10.3 ± 7.6 mm Hg) were free from injury ($p < 0.05$). This study indicates that SNP can increase the risk of neurological injury during aortic operations by reducing spinal cord perfusion pressure. Alternative means of controlling proximal hypertension are recommended.

(Ann Thorac Surg 1989;47:379–83)

Proximal hypertension that follows aortic cross-clamping during repair of thoracic aneurysms is usually controlled with sodium nitroprusside (SNP). Recent experimental reports [1] have suggested that the intraoperative use of SNP might increase the incidence of postoperative paraplegia. The need for maintenance of distal aortic blood pressure with shunts or bypass, once thought to be crucial for the protection of the spinal cord, has recently been challenged in clinical studies [2]. Many investigators have documented that blood supply to the spinal cord is not dependent solely on distal aortic blood pressure (BP). The concept of spinal cord perfusion pressure (SCPP), defined as mean distal aortic BP minus mean cerebrospinal fluid (CSF) pressure, has been introduced as one of the most important determinants of spinal cord integrity during aortic cross-clamping [3–5].

Sodium nitroprusside has been shown to increase intracranial pressure in patients with intracranial lesions [6], but its effects on CSF pressure and spinal cord perfusion have not been studied. If SNP exerts a similar effect in patients undergoing temporary aortic occlusion during repair of thoracic aneurysms, then it would reduce spinal cord perfusion.

This experimental study was designed to investigate the effects of SNP on aortic and spinal fluid dynamics, SCPP, spinal cord blood flow, and the incidence of postoperative paraplegia after temporary aortic occlusion. Somatosensory evoked potentials (SEPs) were monitored in all animals because electrophysiological changes in the spinal cord have been correlated with SCPP [7].

Material and Methods

Twelve mongrel dogs weighing 25 to 30 kg were anesthetized with intravenous administration of Nembutal (pentobarbital sodium) (20 mg/kg) and fentanyl (4 μg/mL). Animals were intubated and placed on a Harvard ventilator utilizing room air. Respirator settings included a tidal volume of 12 mL/kg, a respiratory rate to maintain partial pressure of carbon dioxide between 25 and 35 mm Hg, and 5 cm H_2O of positive end-expiratory pressure. A heating pad and intravenously administered warm fluids

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Table 1. Hemodynamics[a]

	Baseline		Aortic Cross-Clamping	
Variable	Control	SNP	Control	SNP
Proximal BP	108 ± 21	92.0 ± 9	146 ± 14^{b}	99.8 ± 12^{c}
Distal BP	104 ± 22	94.0 ± 14	23.0 ± 7^{b}	11.8 ± 5^{c}
CSFP	9.1 ± 1.3	10.6 ± 1.9	12.9 ± 1.1^{b}	20.1 ± 5.5^{c}
SCPP	94.8 ± 21.3	84.0 ± 13.4	10.3 ± 7.6^{b}	−9.9 ± 6.8^{c}

[a] Data are shown as the mean ± the standard deviation in millimeters of mercury. [b] Significance: $p < 0.005$ versus baseline. [c] Significance: $p < 0.005$ versus control. [d] Significance: $p < 0.05$ versus control.

BP = blood pressure; CSFP = cerebrospinal fluid pressure; SCPP = spinal cord perfusion pressure; SNP = sodium nitroprusside.

were used to maintain normothermia. Pressure-monitoring catheters were inserted into the left subclavian and left femoral arteries and the right jugular vein to monitor aortic pressures proximal and distal to the cross-clamp and central venous pressure. A 20-gauge, 1.5-inch (37.5 mm) spinal needle was percutaneously inserted into the cisterna cerebellomedullaris to monitor CSF pressure. All pressures were monitored with Bentley Trantec physiological pressure transducers (model 60-800; Santa Ana, CA). Intravenous fluids were administered to achieve a central venous pressure of 3 mm Hg, and then were maintained at a rate of 50 mL/kg/h.

Somatosensory evoked potentials (SEPs) were monitored using previously published techniques [8]. The SEP waveforms were recorded every minute during the cross-clamp interval. Loss of SEPs was defined as the time at which the waveform was flat on two successive acquisitions.

Through a left thoracotomy in the fourth intercostal space, the aorta was isolated 1 cm distal to the left subclavian artery. Through a pursestring suture, an Argyle catheter was inserted into the left atrium to inject radiolabeled microspheres. Baseline SEP, proximal and distal aortic pressures, and CSF pressures were acquired after a ten-minute stabilization period. The aorta was then cross-clamped for 30 minutes at the previously isolated site, and the same variables were measured every minute during the experiment. One minute before cross-clamp release, 44.6 mEq of sodium bicarbonate was given intravenously. The animals were then allowed to recover.

Spinal cord blood flow was measured using 15-μm radiolabeled microspheres [(niobium 95, cerium 141, scandium 46, and strontium 85) [9]. Microspheres were injected into the left atrium in a random order at three time intervals: stable baseline, ten minutes after application of the cross-clamp, and five minutes after cross-clamp release. Reference samples were collected through the left carotid line for two minutes.

Twenty-four and 72 hours after the operation, an observer unaware of the experimental protocol graded the gait status using Tarlov's criteria [10]:

Grade 0—spastic paraplegia and no movement of the lower limbs
Grade 1—spastic paraplegia and slight movement of the lower limb joint
Grade 2—good movement of the lower limbs but unable to stand
Grade 3—able to stand but not able to walk normally
Grade 4—complete recovery

Animals were then killed using intravenous administration of pentobarbital followed by a potassium chloride bolus.

After each animal was killed, the spinal cord was removed and divided into two upper "nonischemic" segments (C-1 to C-8, T-1 to T-10) and two lower "ischemic" segments (T-11 to T-13, L-1 to L-3). Radioactivity was counted using a gamma counting system (Nuclear-Chicago), and blood flow was calculated in milliliters per 100 grams of tissue per minute.

In the 6 control animals, no attempt was made to manage proximal hypertension. In the experimental group (n = 6), SNP (150 mg in 250 mL of 5% dextrose in water) was used to decrease the mean proximal BP to approximately 100 mm Hg during the cross-clamp interval.

All experimental animals received humane care and treatment in compliance with the "Guide for the Care and Use of Laboratory Animals" published by the National Institutes of Health (NIH Publication No. 85-23, revised 1985).

All data are reported as the mean ± the standard deviation, and were analyzed with Fisher's exact test and Student's t test. Statistical significance was accepted at a p value of less than 0.05.

Results

Hemodynamics

There was no significant difference in proximal or distal blood pressure or CSF pressure between the two groups at baseline (Table 1). During the cross-clamp interval, the mean proximal aortic pressure in the control group rose from 108 ± 21 to 146 ± 14 mm Hg ($p < 0.001$), whereas the mean BP in the SNP group was maintained at 99.8 ± 12 mm Hg (p = not significant compared with baseline BP)

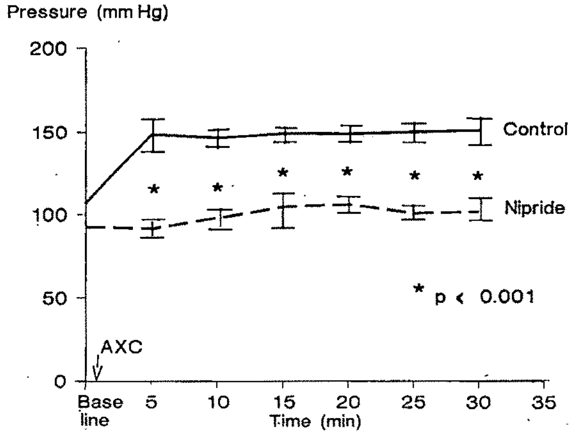

Fig 1. Comparison of proximal blood pressure between control and sodium nitroprusside (Nipride) animals at baseline and during the aortic cross-clamp (AXC) interval.

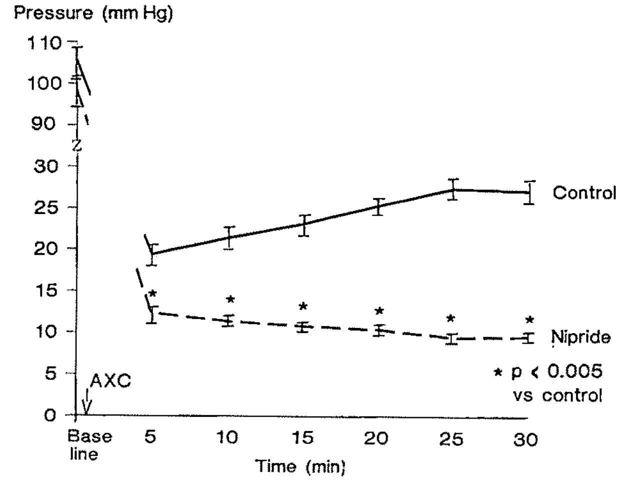

Fig 2. Comparison of distal blood pressure between control and sodium nitroprusside (Nipride) *animals at baseline and during the aortic cross-clamp* (AXC) *interval.*

(Fig 1). Mean distal aortic pressure decreased from systemic values to 23 ± 7 mm Hg in control animals and to 11 ± 5 mm Hg in the SNP group ($p < 0.005$) (Fig 2). Cerebrospinal fluid pressure increased significantly from 9.1 ± 1.3 to 12.9 ± 1.1 mm Hg in controls ($p < 0.005$) and from 10.6 ± 1.9 to 20.1 ± 5.5 mm Hg in the SNP group ($p < 0.005$) (Fig 3). Negative SCPPs were observed in the latter group (−9.9 ± 6.8 mm Hg), whereas control animals displayed positive and significantly greater perfusion pressures (+10.3 ± 7.6 mm Hg) ($p < 0.05$) (Fig 4).

Neurological Injury

There was a significant difference in the neurological injury sustained in the two groups (Fig 5). All animals in the control group had complete recovery, Tarlov's grade 4, except for 1 animal who had a slight limp and was graded 3. This animal had an SCPP of +2.3 mm Hg, whereas other animals in the control group had perfusion pressures of 5 mm Hg or greater. Animals in the SNP group uniformly sustained spastic paraplegia (6 of 6).

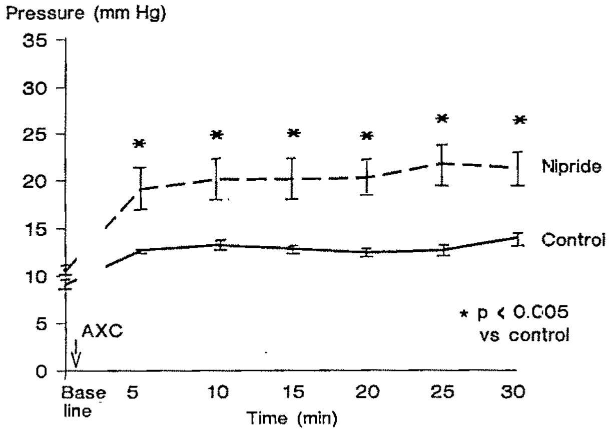

Fig 3. Comparison of cerebrospinal fluid pressure between control and sodium nitroprusside (Nipride) *animals at baseline and during the aortic cross-clamp* (AXC) *interval.*

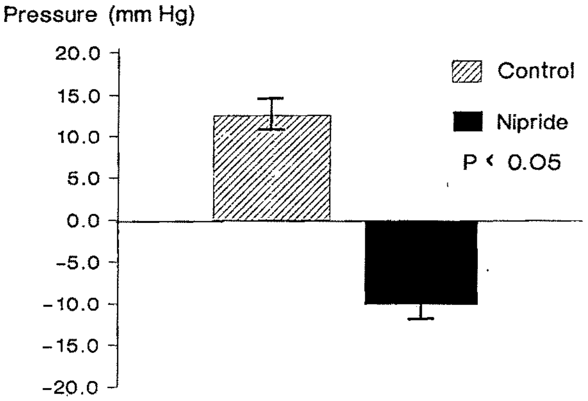

Fig 4. Mean spinal cord perfusion pressure of control and sodium nitroprusside (Nipride) *animals during the aortic cross-clamp interval.*

Blood Flow

Spinal cord blood flow was analyzed in 4 control animals and 5 animals in the SNP group (Table 2). Baseline blood flows in the upper (C-1 to T-10) and lower (T-11 to L-3) cord segments were not significantly different between the two groups. During the cross-clamp interval, animals receiving SNP displayed a decrease in blood flow to the lower spinal cord segment compared with controls (5.8 ± 6.3 versus 1.7 ± 2.7 mm Hg, $p = 0.09$). Conversely, SNP infusion increased blood flow to the upper cord segments compared with controls (6.3 ± 4.3 versus 13.3 ± 9.0 mm Hg; $p = 0.06$).

Somatosensory Evoked Potential Changes

The use of SNP was associated with an early loss of SEPs (3 minutes 32 seconds). In control animals, SEP loss occurred significantly later (11 minutes 1 second) ($p < 0.05$).

Comment

Several factors appear to be related to the occurrence of postoperative paraplegia during resection of thoracic and

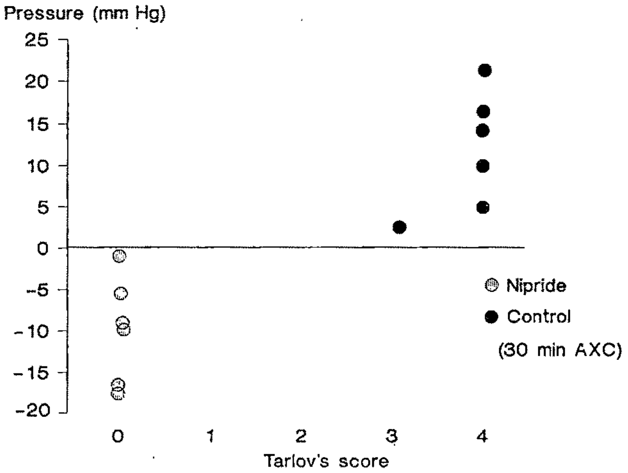

Fig 5. Spinal cord perfusion pressure versus neurological outcome (Tarlov's score [10]) in control and sodium nitroprusside (Nipride) *animals.* (AXC = *aortic cross-clamping.*)

Table 2. Spinal Cord Blood Flow[a]

	Upper Cord		Lower Cord	
Time	Control	SNP	Control	SNP
Baseline	12.4 ± 4.10	11.5 ± 6.1	18.5 ± 10.9	16.0 ± 5.2
Aortic cross-clamping	6.30 ± 4.30	13.3 ± 9.0[b]	5.80 ± 6.30	1.70 ± 2.7[c]
Reperfusion	16.4 ± 14.2	41.6 ± 34.6[d]	65.3 ± 40.4	57.4 ± 49.2

[a] Data are shown as the mean ± the standard deviation in milliliters per 100 grams per minute. [b] Significance: $p = 0.06$ versus control. [c] Significance: $p = 0.09$ versus control. [d] Significance: $p = 0.07$ versus control.

Lower cord = T-11 to L-3; SNP = sodium nitroprusside; upper cord = C-1 to T-10.

thoracoabdominal aneurysms: cross-clamp interval, extent of the aneurysm, dissection, age of the patient, reimplantation of intercostal and lumbar arteries, intraoperative hypotension, and degree of collateralization [11, 12]. Experimental and clinical investigations have shown that SCPP is a very important determinant of spinal cord protection [3–5]. Cerebrospinal fluid pressure, one of the two determinants of SCPP (mean distal aortic BP − CSF pressure) has been shown to be related to systolic BP, CSF pH, and intracerebral blood volume [13], and it may be affected by several pharmacological as well as anesthetic agents [14].

Factors affecting either the distal aortic BP or CSF pressure can influence SCPP. It appears from experimental and clinical work that an SCPP lower than one might expect is required to protect the spinal cord. We [7] have shown in previous work that the critical level of SCPP in dogs is 11 mm Hg. Blaisdell and Cooley [3] demonstrated that an SCPP of 12 to 14 mm Hg reduced the incidence of paraplegia in an animal model, and Miyamoto and coworkers [5] reported that 15 mm Hg is adequate to prevent paraplegia in patients. Therefore, it is of the utmost importance that both determinants of SCPP be constantly monitored and, at the same time, that every factor that can affect either of these two variables be taken into consideration.

In our study, the infusion of SNP effectively controlled proximal BP after the application of the aortic cross-clamp, but in the control animals, proximal BP rose significantly from 108 to 146 mm Hg ($p < 0.001$). There was a significant difference in distal aortic BP between the two groups after placement of the aortic cross-clamp. Distal aortic pressure decreased from systemic values to 23 mm Hg in the control group and to 11 mm Hg in the SNP group. The much lower distal BP in the latter group can be explained by the decrease in proximal BP and distal vasodilation induced by SNP.

Analysis of CSF pressures showed that there was a significant rise in CSF pressure in both groups: from 9.1 to 12.9 mm Hg in the controls ($p < 0.005$) and from 10.6 to 20.1 mm Hg in the SNP group ($p < 0.005$). The small rise in CSF pressure after application of the aortic cross-clamp in control animals resulted from the uncontrolled proximal hypertension. On the other hand, as the proximal BP in the SNP group was controlled to a mean of 100 mm Hg, the significant increase in CSF pressure must have been the result of a different mechanism. Understanding the increase in CSF pressure produced by the infusion of SNP is of crucial importance, because aortic cross-clamping decreases distal aortic BP to low values; thus, any increase in CSF pressure decreases SCPP below the relatively low threshold pressure necessary for the preservation of spinal cord integrity.

Sodium nitroprusside increases cerebrovascular blood flow [15], probably through a loss of autoregulation, and at the same time increases the blood flow to the upper segments of the spinal cord (nitroprusside steal phenomenon) [12]. Autoregulation of the cerebral and spinal vasculature is the property that maintains a constant blood flow as perfusion pressure changes. Normally in dogs, cerebral and spinal cord blood flow remain constant between a mean BP of 60 and 120 mm Hg [16]. If autoregulation is lost, the increased cerebrovascular volume associated with a decreased intraspinal cord compliance leads to increased CSF pressures [16]. The reduction in SCPP to +10.3 in the controls and −9.9 mm Hg in the SNP group was the result of a decrease in distal aortic BP and a simultaneous increase in CSF pressure.

Because we did not drain CSF in this experiment, we cannot tell whether the increase in CSF pressure resulted from an increase in the production of CSF or an increase in the spinal cord volume with consequent decrease in the compliance of the spinal canal. The magnitude of the increase in CSF pressure in the SNP group may have been partially affected by our decision to maintain the mean proximal BP at 100 mm Hg. Lowering the proximal BP to 80 to 85 mm Hg might have reduced the magnitude of the rise in CSF pressure. However, as the reduction in proximal BP would have been associated with lower distal aortic BP, the net effect on SCPP may not have changed.

The analysis of blood flows of the spinal cord in the two groups confirmed the results of Gelman and colleagues [17]. The infusion of SNP increased blood flow to the upper cord segments (C-1 to T-10) during aortic cross-clamping compared with controls. The increase in blood flow of the upper cord segments approached significance. However, it was not possible to document a significant decrease in blood flow to the lower segments (T-11 to L-3) of the spinal cord when SNP was infused, despite a negative SCPP. The radiolabeled microsphere method may not be sensitive enough to detect differences at very low flow rates.

All animals in the SNP group had a negative SCPP and spastic paraplegia, whereas animals in the control group with an SCPP greater than 5 mm Hg were neurologically intact. In this latter group, 1 animal with an SCPP of 2.3 mm Hg was graded 3 by the criteria of Tarlov [10]. Our previous work [7] showed that an SCPP of 10 mm Hg is the threshold value for maintaining spinal cord integrity for a 40-minute cross-clamp interval; the shorter cross-clamp interval of 30 minutes in this experiment may explain why the animal with an SCPP of 2.3 mm Hg did not become paralyzed. In clinical practice, we can monitor SCPP only by simultaneously monitoring distal aortic pressure and CSF pressure. However, the relationship between SCPP and spinal cord blood flow is not yet well established. It would be optimal to have a means of monitoring actual blood flow to the spinal cord when the aorta is cross-clamped because, as recently documented by Crawford and associates [2], even a reasonably high perfusion pressure (> 60 mm Hg) while on left atrium–femoral artery bypass may not always protect the spinal cord from injury.

Somatosensory evoked potential changes were different in the two groups. The loss in SEPs occurred significantly earlier (3 minutes 32 seconds) in the SNP group compared with control animals (11 minutes 1 second). The loss of SEP tracing after 11 minutes was associated with absence of neurological injury, thus confirming our previous finding [7] that in the dog model, this is the critical time for prediction of neurological outcome. The differences in SEP changes were due to the differences in SCPP, once again indicating that the electrophysiological changes in the spinal cord are related to ischemia.

This study has documented the deleterious effects of the infusion of SNP on SCPP and paraplegia in an animal model. Consequently, we advocate the use of left atrium–femoral artery bypass to provide adequate distal perfusion to the spinal cord and to minimize the use of vasodilators by adjusting the flow rate of the pump [18]. Although shunts can provide equal distal perfusion compared with either femorofemoral or left atrium–femoral artery bypass, they do not provide similar control of proximal hypertension during temporary occlusion of the thoracic aorta. The use of vasodilators to control the proximal hypertension that follows aortic cross-clamping should probably be limited to those few instances in which left atrium–femoral artery bypass cannot be used because of the extensiveness of the aneurysm and the limited distal vascular bed that does not allow the high flow rates necessary for adequate proximal unloading.

Based on the results of the present study, we believe that it may be appropriate to consider the use of partial exsanguination when left atrium–femoral artery bypass cannot be used or when the necessary flow rates are limited, rather than the use of vasodilators, which have a negative impact on SCPP. A potential additional advantage of this method is that reinfusion of the whole blood might reverse some of the coagulation problems associated with operation on the thoracic aorta. The hemodilution resulting from this technique might also improve the blood supply to the spinal cord because of improved rheology. Further work should investigate the effects of drainage of CSF on SCPP when SNP is used to control proximal BP during aortic cross-clamping.

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Postoperative Conduction Disturbances: A Comparison of Blood and Crystalloid Cardioplegia

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Conduction system disturbances after cardioplegia are well described. Our four-man group changed in mid-1987 from standard crystalloid cardioplegia (35 mEq/L of KCl) to blood cardioplegia (4 parts blood to 1 part cardioplegia) (18 mEq/L of KCl) based on experimental and clinical evidence that blood cardioplegia provides better myocardial protection. Shortly thereafter, we anecdotally noted increased conduction abnormalities. This prompted us to compare serially all patients undergoing coronary artery bypass grafting during 1987 for perioperative and late conduction system disturbances after either crystalloid or blood cardioplegia. Surgeons and techniques including topical cooling did not differ. Forty-one (23%) of 179 patients with crystalloid cardioplegia had conduction disturbances versus 141 (49%) of 289 patients with blood cardioplegia ($p < 0.001$). Perioperative complete heart block requiring atrioventricular sequential pacing occurred in 20 patients with crystalloid cardioplegia versus 67 patients with blood cardioplegia ($p < 0.002$), and atrioventricular block requiring permanent pacing was present in 4 and 12 patients ($p < 0.001$), respectively. Left bundle-branch block was found in 8 patients given crystalloid cardioplegia and 28 patients with blood cardioplegia ($p < 0.05$); right bundle-branch block, 12 and 68 patients ($p < 0.001$); left anterior hemiblock, 8 and 37 patients ($p < 0.001$); and interventricular conduction delay, 15 and 53 patients ($p < 0.005$), respectively. Bifascicular block occurred in 4 patients receiving crystalloid cardioplegia versus 23 receiving blood cardioplegia ($p < 0.001$). There was no difference in cross-clamp times, number of grafts, or amount of cardioplegic solution between patients with and patients without conduction disturbances within each group. Except for perioperative complete heart block, most conduction disturbances were present at discharge. We conclude that the use of blood cardioplegia is associated with significantly more postoperative conduction disturbances than is the use of crystalloid cardioplegia. This suggests that patients with preexisting conduction defects should not receive blood cardioplegia. Further investigation is indicated to confirm and elucidate the causes of this phenomenon.

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Conduction disturbances after coronary artery bypass grafting are well described; they occur in as few as 18% and as many as 45% of patients [1–5]. Although comparisons exist between the conduction disturbances observed with crystalloid cardioplegia versus cold fibrillatory arrest [2] and in the incidence of conduction disturbances following blood cardioplegia [1], we are aware of no studies that compare conduction disturbances between crystalloid and blood cardioplegic solutions.

In the middle of 1987, our four-man group of cardiac surgeons changed from crystalloid cardioplegia to blood cardioplegia as our preferred method of myocardial protection. Shortly thereafter, we anecdotally noted a substantial increase in perioperative and late conduction disturbances in those patients receiving blood cardioplegia. This finding prompted a complete review of all patients undergoing cardiopulmonary bypass from September 1986 to December 1987 in an effort to compare conduction disturbances between crystalloid and blood cardioplegia.

Material and Methods

A total of 468 patients underwent simple coronary artery bypass grafting over the 15-month study; 179 patients received crystalloid cardioplegia and 289, blood cardioplegia. All patients undergoing coronary bypass grafting were included in the study, even those with preoperative conduction disturbances. All four functional classes were represented. No patient was excluded on the basis of elective versus urgent operation.

Surgical Technique

All coronary artery bypass operations were performed by or under the direction of four senior surgeons at the University of Maryland Hospital. All patients had preoperative placement of thermodilution Swan-Ganz catheters and arterial monitoring catheters. Cardiopulmonary bypass was instituted using a dual-stage venous cannula by two surgeons; the other surgeons used two venous cannulas in the majority of their operations. After the initiation of cardiopulmonary bypass, three surgeons routinely vented the left ventricle through the right superior pulmonary vein; one surgeon continuously monitored left atrial pressure and vented only as necessary. Rectal or

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Table 1. Incidence of Conduction Disturbances Versus Type of Cardioplegia[a]

Cardioplegia	No. of Patients With Disturbance	Type of Conduction Disturbance						
		Periop CHB	Permanent CHB	RBBB	LBBB	LAHB	IVCD	BFB
Crystalloid (30 mEq KCl/L) (n = 179)	41 (23)	20 (11)	4 (2)	12 (7)	8 (4)	8 (4)	15 (8)	4 (2)
Blood (18 mEq KCl/L) (n = 289)	141 (49)	67 (23)	12 (4)	68 (24)	28 (10)	37 (13)	53 (18)	23 (8)
Significance	$p < 0.001$	$p < 0.002$	$p < 0.001$	$p < 0.001$	$p < 0.05$	$p < 0.01$	$p < 0.005$	$p < 0.001$

[a] Numbers in parentheses are percentages.

BFB = bifascicular block; CHB = complete heart block; IVCD = interventricular conduction delay; LAHB = left anterior hemiblock; LBBB = left bundle-branch block; RBBB = right bundle-branch block.

bladder temperature was lowered to 26° to 30°C during the course of the bypass procedure in each patient.

After aortic cross-clamping, either crystalloid or blood cardioplegia was infused into the aortic root at approximately 10 to 12 mL/kg as an initial dose, with infusion pressure monitored by the perfusionist. Topical hypothermia in the form of slushed ice from normal saline solution was used by all surgeons. The crystalloid cardioplegia used in 179 patients was prepared in the University of Maryland Hospital pharmacy from 1,000 mL of Plasmalyte (Abbott Laboratory) to which was added 30 mEq of KCl, 100 mg of CaCl, 2,500 units of heparin sodium, 75 mEq of sodium bicarbonate, and 30 mL of 50% dextrose in water, resulting in a final potassium concentration of approximately 35 mEq/L.

To obtain blood cardioplegia, the identical crystalloid solution was utilized; however, an additional 40 mEq of KCl was added, making the total KCl concentration in the solution 75 mEq of KCl per liter. Blood cardioplegia was delivered through a BCD system (Shiley Incorporated) in a 4:1 blood to crystalloid cardioplegia mixture with a resultant delivered potassium concentration of 18 mEq/L. Blood cardioplegia was usually administered as an initial bolus of 10 to 15 mL/kg.

Distal anastomoses were usually accomplished in the order of severity of lesions, except when the internal mammary artery was used. In that case, the internal mammary artery was normally placed to the most important vessel or vessels on the anterior surface of the left ventricle as the last anastomosis. After each distal vein graft anastomosis, approximately 50 to 100 mL of cardioplegic solution or iced pump blood without additives was instilled down the vein graft. After every 20 to 30 minutes of cross-clamp time or whenever the myocardial temperature had risen above 15°C, 300 to 500 mL of cardioplegic solution was reinstilled into the aortic root. All reinfusion cardioplegic solutions contained the original potassium concentration.

Patient rewarming was usually begun at the start of the final distal anastomosis. After completion of all distal anastomoses, the aortic cross-clamp was removed, and if required, the heart was defibrillated. A partial occluding clamp was applied to the ascending aorta during rewarming; the proximal anastomoses were performed and air was removed from them after removal of the partial occluding clamp.

If the ventricle was quiescent during the rewarming period, pacing was, in general, not instituted until the left ventricular vent was removed or until the patient was prepared for weaning from bypass. All patients had at least one atrial and one ventricular temporary pacing electrode attached to the myocardium. All patients with perioperative complete heart block were weaned from cardiopulmonary bypass using atrioventricular sequential pacing.

A 12-lead electrocardiogram (ECG) was obtained approximately two hours postoperatively in the intensive care unit and daily thereafter for four days. A final ECG was obtained for review of conduction disturbances at the time of discharge. All ECGs had an initial computerized program interpretation followed by interpretation by a fellow in cardiology and an attending professor of cardiology. Conduction disturbances were classified as either third-degree atrioventricular block (complete heart block), left bundle-branch block, right bundle-branch block, left anterior hemiblock, nonspecific interventricular conduction delay, or the combination of right bundle-branch block and left anterior hemiblock (bifascicular block).

Statistical Analysis

Comparisons were made between patients receiving blood cardioplegia and patients receiving crystalloid cardioplegia using Student's t test and χ^2 analysis. A p value of less than 0.05 was considered significant.

Results

One or more types of conduction disturbance developed during the perioperative period in 41 (23%) of 179 patients receiving crystalloid cardioplegia compared with 141 (49%) of 289 patients receiving blood cardioplegia ($p < 0.001$). Comparison was made within the two cardioplegia groups between patients with and patients without conduction disturbances and between the two cardioplegia groups to determine which factors contributed to the conduction disturbance (Table 1). Temporary complete heart block extending at least one hour postoperatively occurred in 20 crystalloid cardioplegia patients (11%) versus 67 blood cardioplegia patients (23%) ($p < 0.002$). Placement of transvenous permanent pacemakers was required in 4 patients in the former group and 12 in the latter group ($p < 0.001$).

Table 2. Relationship Between Type of Cardioplegia, Conduction Disturbances, and Operative Variables[a]

Cardioplegia	Age (yr)	Grafts/ Patient	Cross-Clamp Time (min)	Total Cardioplegia (mL)
Crystalloid				
With CD	62 ± 10	3.1 ± 1	53 ± 16	1,577 ± 364
Without CD	64 ± 8	3.1 ± 1	48.5 ± 14	1,475 ± 406
Blood				
With CD	63 ± 9[b,c]	3.5 ± 1[b,c]	58.1 ± 17[b,c]	2,334 ± 645[b,c]
Without CD	61 ± 11[b,c]	3.6 ± 1[b,c]	57.0 ± 18[b,c]	2,150 ± 690[b,c]

[a] Data are shown as the mean ± standard deviation. [b] Significance: p = not significant, blood versus crystalloid cardioplegia. [c] Significance: p = not significant, with versus without conduction disturbance.

CD = conduction disturbance.

Right bundle-branch block was the most common conduction abnormality, occurring in 12 crystalloid cardioplegia patients (7%) and 68 blood cardioplegia patients (24%) ($p < 0.001$). Interventricular conduction delay occurred in 8% of patients with crystalloid cardioplegia and 18% of those with blood cardioplegia ($p < 0.005$). Left anterior hemiblock was noted in 4% of crystalloid cardioplegia patients versus 13% of blood cardioplegia patients ($p < 0.001$). Left bundle-branch block developed in 4% of patients given crystalloid cardioplegia and 10% of patients given blood cardioplegia ($p < 0.05$). Bifascicular block occurred in 2% of patients with crystalloid cardioplegia and 8% of those given blood cardioplegia ($p < 0.001$) (see Table 1).

The mean age of patients in whom conduction disturbances developed after crystalloid cardioplegia was 62 years; this was not significantly different from the mean age of the crystalloid cardioplegia patients without associated disturbances (64 years). Neither of these ages differed from the mean age of blood cardioplegia patients without conduction disturbances (61 years) or the mean age of blood cardioplegia patients with conduction abnormalities (63 years). Hence, there were no significant age differences within groups or between groups (Table 2). Among the 29 patients 70 years old or older who received crystalloid cardioplegia, conduction disturbances developed in 41%; conduction disturbances occurred in 66% of blood cardioplegia patients in the same age group (p = not significant [NS]) (Table 3).

Crystalloid cardioplegia patients had a mean of 3.1 bypass grafts per patient in both subgroups (with and without conduction disturbances). This did not differ significantly from the mean number of grafts per patient in the blood cardioplegia group or subgroups (see Table 2). Fourteen crystalloid cardioplegia patients received five or more bypass grafts; conduction defects developed in only 2. Forty-five blood cardioplegia patients had five or more grafts; conduction defects developed in 23 (see Table 3). These ratios were less than for the groups as a whole.

A mean of 1,475 mL of crystalloid cardioplegia was given to patients without conduction abnormalities versus 1,577 mL to patients with conduction abnormalities (p = NS). A total of 2,150 mL of blood cardioplegia was given to patients who did not have conduction defects, and 2,334 mL was received by patients in whom defects developed (p = NS). There was no significant difference between the amount of cardioplegia given to the crystalloid cardioplegia patients versus the blood cardioplegia patients (see Table 2).

More than 3,000 mL of blood cardioplegia was used in 38 patients. Conduction disturbances developed in 24 (63%) of them, but this number was not significantly different from the blood group as a whole ($p = 0.06$). Patients receiving 2,000 to 2,499 mL of blood cardioplegia had a 77% incidence of disturbances, whereas those receiving less than 2,000 mL had an incidence of only 44%. Only 49% of patients receiving 2,500 to 2,999 mL of blood cardioplegia had conduction disturbances. Moreover, if the amount of potassium is considered, crystalloid cardioplegia patients received a mean total dose of 45 mEq of potassium in the solution versus only 40 mEq for blood cardioplegia patients (p = NS).

Among patients receiving crystalloid cardioplegia, 13 with perioperative complete heart block ultimately had resolution of this temporary abnormality with no residual conduction defect; 7 subsequently had resolution but were left with a residual conduction defect. In contrast, 23 blood cardioplegia patients had resolution of perioperative complete heart block without underlying conduction disturbance, and 44 patients were left with an underlying conduction defect after resolution of the complete heart block ($p < 0.01$) (Table 4).

Mean aortic cross-clamp time in crystalloid cardioplegia patients without defects was 48.5 minutes versus 53 minutes for crystalloid cardioplegia patients with defects (p = NS). Blood cardioplegia patients without conduction defects had aortic cross-clamp times of 57 minutes versus 58 minutes for patients with block (p = NS) (see Table 2). Fourteen crystalloid cardioplegia patients and 67 blood

Table 3. Relationship Between Type of Cardioplegia and Conduction Disturbance in Association With Other Factors[a]

	Factors			
Cardioplegia	≥5 Grafts/Patient	Age ≥ 70 Years	Cross-clamping ≥70 Minutes	All Patients With Conduction Disturbance
Crystalloid	2/14 (14)	12/29 (41)	4/14 (29)	41/141 (29)
Blood	23/45 (51)[b]	39/59 (66)	33/67 (49)[b]	141/289 (49)[b]

[a] Numbers in parentheses are percentages. [b] $p < 0.05$, blood versus crystalloid cardioplegia.

Table 4. Relationship Between Type of Cardioplegia and Conduction Disturbance[a]

Cardioplegia	Perioperative Complete Heart Block	Residual Conduction Disturbance	Initial Conduction Disturbance	Conduction Disturbance Resolved at Discharge
Crystalloid	20	7 (35)	41	8 (20)
Blood	67	44 (66)	141	10 (7)
Significance		$p < 0.01$		$p < 0.02$

[a] Numbers in parentheses are percentages.

cardioplegia patients had cross-clamp times of 70 minutes or more; conduction disturbances developed in 29% of the former versus 49% of the latter (see Table 3). These ratios are no different for the group as a whole.

Five patients in the crystalloid cardioplegia group had preexisting conduction defects. None of these patients sustained additional conduction defects or complete heart block in the perioperative period. On the other hand, in 1 patient receiving blood cardioplegia who had preoperative left anterior hemiblock, complete heart block developed, necessitating permanent pacing postoperatively.

Forty-one crystalloid cardioplegia patients had conduction defects that persisted beyond the perioperative complete heart block. Of these, 8 had resolution before discharge. In comparison, only 10 of the 141 blood cardioplegia patients with conduction disturbances had resolution in the postoperative period ($p < 0.02$) (see Table 4). Eighty (45%) of the 179 patients receiving crystalloid cardioplegia required one or more inotropic agents in the postoperative period versus 111 (38%) of the 289 patients receiving blood cardioplegia (p = NS).

Comment

Although conduction abnormalities after coronary bypass operations have been recognized for the last several years, the causes of these conduction defects are still not well known. It appears that approximately 20% of patients can be expected to have new conduction defects after receiving crystalloid cardioplegia and, based on the only other study of blood cardioplegia, approximately 50% of patients receiving it can be expected to have new conduction disturbances postoperatively [1–5].

The effect of cardioplegic arrest on the conduction system of the heart is well known. O'Connell and colleagues [5] demonstrated that transient bundle-branch blocks developed in 34% of crystalloid cardioplegia patients compared with only 6% of patients who had cold fibrillatory arrest as the method of myocardial protection. These authors also demonstrated that these conduction disturbances were not related to perioperative myocardial infarction. Sharma, Wexelman, Zeldis, and their coworkers [2–5] demonstrated an approximately 20% incidence of bundle-branch block after crystalloid cardioplegia; however, no consensus could be reached as to the cause of these disturbances. The type of bundle-branch block reported also varied widely; one series reported no right bundle-branch block, whereas another series reported right bundle-branch block as the predominant lesion [3, 4].

Baerman and colleagues [1] at the University of Michigan recently described a large number of conduction disturbances after blood cardioplegia, but did not compare, in any controlled fashion, this increase to the incidence with crystalloid cardioplegia. They thought that the disturbances correlated with the number of arteries bypassed and, as a corollary, to the aortic cross-clamp time. In our study, we could find no evidence that patient age, number of bypass grafts, or amount of cardioplegic solution correlated with the incidence of postoperative conduction disturbances. Indeed, the only differences in conduction defects that we were able to determine could be attributed directly to the use of blood cardioplegia. Moreover, the impressive extent of conduction disturbances with blood cardioplegia seen in our study are identical to those found in the Michigan study.

The mechanism by which blood cardioplegia produces more conduction disturbances is, as yet, unknown. Considerable interest has been generated in regard to the amount of potassium present in cardioplegic solutions and its effect on conduction. Indeed, in the study of Baerman and associates [1], potassium was deliberately kept out of all subsequent cardioplegia infusions because of the presumed danger of high-potassium cardioplegia in producing heart block. This impression has been present ever since the development of the Melrose solution [6].

The association of high potassium concentration and complete heart block or conduction disturbances in the postoperative period is an ongoing investigative problem. Ellis and colleagues [7] have shown that major atrioventricular dissociation arrhythmias could be avoided by using an initial infusion of 20 mEq/L of KCl, followed by repeated infusions of normal concentrations of potassium. Ferguson and colleagues [8–10] found that higher potassium concentrations appeared to provide better protection of the conduction system. Smith and associates [11] determined that 15 mEq of KCl per liter afforded the best protection of the conduction system, whereas 5 or 25 mEq/L of KCl led to more conduction disturbances. Ferguson and co-workers [12] further demonstrated that reinfusion of hypercalcemic rather than normal calcemic cardioplegic solutions and the application of topical hypothermic techniques led to the ablation or decrease of low-amplitude electrical activity during the period of cardioplegic arrest. Unfortunately, all of these studies were conducted using crystalloid cardioplegia.

Both clinically and experimentally, it appears that concentrations of potassium in the range of 18 mEq/L, as was used in our blood cardioplegia, would not be expected alone to produce major conduction disturbances. Conversely, our crystalloid cardioplegia potassium concentration of 35 mEq/L could be said to be on the high limits of recommended doses and might be expected to produce more conduction defects. The fact that there were significantly fewer conduction defects with crystalloid cardioplegia points to the fact that potassium per se was not the principal cause of the postoperative defects seen in our study. This is substantiated by the study by Baerman and colleagues [1] in which no KCl was added to subsequent blood cardioplegia infusions, yet a large number of defects resulted.

Additional arguments have been proposed that suggest that at very low temperatures, blood undergoes rouleaux formation with potential capillary plugging; whether this causes localized ischemia of the conduction system is not known. Because of its higher viscosity, blood cardioplegia may be distributed less well to ischemic areas of the heart. Hence, patients with blood cardioplegia might be expected to have poorer postoperative hemodynamic outcomes, a fact that was not borne out by this study. Indeed, despite more grafts and longer cross-clamp times, fewer blood cardioplegia patients needed inotropic agents than their crystalloid cardioplegia counterparts. Last, studies must be undertaken that look at lower blood to crystalloid mixing ratios (1:1, 2:1, or 3:1) to determine if red cell mass is the critical factor in producing conduction defects.

Conclusion

On the basis of our study of 468 consecutive patients undergoing coronary artery bypass grafting, we conclude that the use of blood cardioplegia is associated with significantly more perioperative and postoperative conduction disturbances than is the use of crystalloid cardioplegia. Not only do the conduction disturbances occur significantly more often, but the incidence of complete heart block requiring a permanent pacemaker is double that of crystalloid cardioplegia. Although a number of crystalloid cardioplegia conduction disturbances resolved before discharge, very few conduction disturbances caused by blood cardioplegia similarly disappeared before discharge. In this study, temporary complete heart block in the first hour after cardiopulmonary bypass was a good indicator of permanent conduction disturbance in blood cardioplegia patients, a finding not associated with crystalloid cardioplegia.

Last, the use of crystalloid cardioplegia did not worsen conduction abnormalities present preoperatively, whereas blood cardioplegia produced complete heart block in the presence of left anterior hemiblock in 1 patient. We recommend that blood cardioplegia not be used in the presence of preoperative conduction defects because of the potential for complete heart block in the postoperative period. Further studies are indicated to elucidate the exact mechanism of the production of postoperative conduction disturbances by blood cardioplegia.

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DISCUSSION

DR RICHARD D. WEISEL (Toronto, Ontario, Canada): I compliment the authors on an excellent presentation. They report a high incidence of conduction abnormalities after blood cardioplegia. Their study was disturbing to the 16 cardiac surgeons in Toronto because we all use blood cardioplegia. I was asked to review our data to determine whether we should change our technique of myocardial protection.

We have performed four prospective randomized trials comparing blood with crystalloid cardioplegia. In our study conducted in 1985 (J Thorac Cardiovasc Surg 1987;94:558–65) we reported a 15% incidence of perioperative atrioventricular pacing after both blood and crystalloid cardioplegia (Fig 1). This spring at the meeting of the Western Thoracic Surgical Association, we reported another prospective randomized trial comparing blood

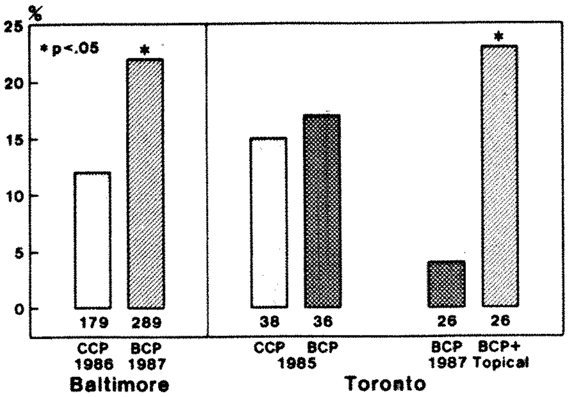

Fig 1. Perioperative atrioventricular pacing. (BCP = *blood cardioplegia;* CCP = *crystalloid cardioplegia.)*

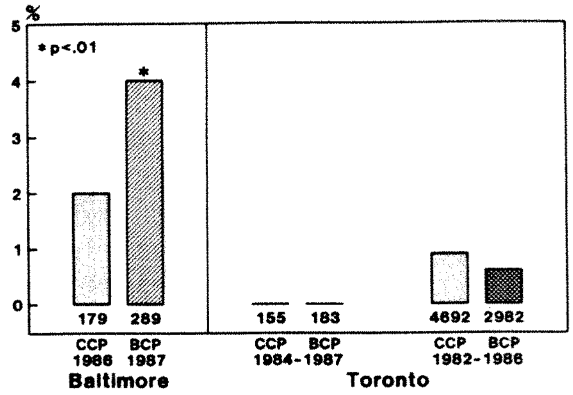

Fig 3. Permanent atrioventricular pacing. (BCP = *blood cardioplegia;* CCP = *crystalloid cardioplegia.)*

cardioplegia with blood cardioplegia augmented by topical iced saline slush. Dr Gundry and his colleagues in Baltimore also employed saline slush with blood cardioplegia. We found that profound cardiac hypothermia induced a 23% incidence of atrioventricular pacing, which was similar to the incidence reported from Baltimore. Therefore, we do not recommend the use of ice slush for elective coronary bypass operations. Lowering the myocardial temperature below 10°C also had detrimental effects on myocardial metabolism and ventricular function.

We evaluated the incidence of perioperative conduction defects (Fig 2). We found a 20% incidence of transient conduction blocks after both blood and crystalloid cardioplegia. However, the addition of iced saline slush increased the incidence of conduction defects to 26%, which was less than the 49% incidence found in Baltimore. Therefore, we recommend continuous monitoring to maintain the myocardial temperatures between 10°C and 15°C to avoid postoperative conduction defects. However, a study from the University of Michigan (Ann Thorac Surg 1987;44:150–3) suggested that the long-term effects of a right bundle-branch block were benign, and clinically relevant complications were rare with this conduction defect.

Therefore, we believe that blood cardioplegia provides better protection than crystalloid cardioplegia. We have demonstrated better myocardial metabolic and ventricular functional recovery after elective coronary bypass surgery (J Thorac Cardiovasc Surg 1984;88:726–41), and we have demonstrated a lower morbidity and mortality in patients who required urgent revascularization for unstable angina (J Vasc Surg 1986;3:764–72). We did not demonstrate an increased risk of perioperative atrioventricular conduction defects or an increased incidence of temporary atrioventricular pacing when iced saline slush was not employed.

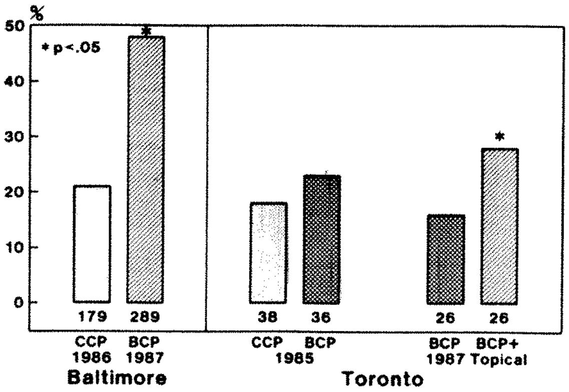

Fig 2. Perioperative conduction blocks. (BCP = *blood cardioplegia;* CCP = *crystalloid cardioplegia.)*

The increasing use of mammary arteries as bypass conduits has reduced our ability to deliver cardioplegic solutions to the anterior surface of the myocardium. Therefore, improved methods of myocardial protection are required. We are investigating retrograde techniques for cardioplegic protection to better protect the heart during coronary bypass operations.

We were very disturbed with the high incidence of permanent pacing in the Baltimore report. Between 1984 and 1987, we randomized 338 patients to either blood or crystalloid cardioplegia (Fig 3), and none of these patients required a permanent pacemaker before, during, or after their coronary bypass procedure. Therefore, we reviewed the need for permanent pacing among the 7,674 consecutive patients who underwent isolated coronary bypass surgery at the University of Toronto between 1982 and 1986. The incidence of permanent pacemaker insertion either before, during, or after coronary bypass grafting was less than 0.8% after either blood or crystalloid cardioplegia. Therefore, I would like to ask Dr Gundry why he inserted so many permanent pacemakers.

DR WATTS R. WEBB (New Orleans, LA): My colleagues and I were intrigued by this paper, and I enjoyed the opportunity of reviewing the manuscript. I must say that I still don't know the answer for the difference in our experiences.

We have not been able to compare crystalloid cardioplegia simultaneously with blood cardioplegia, because we have not used crystalloid cardioplegia since we switched to blood cardioplegia some years ago when the commercial apparatus became available for us to do so, and the patient mix has so completely changed that it wouldn't be fair to compare the two groups. At this moment, for example, we operate on nearly one fourth of our patients very early for acute ischemia or recent myocardial infarction, and about 4% for angioplasty failures or catastrophes.

I have not looked up the total experience, but just in our last 100 patients we found only one transient atrioventricular block, compared with about 23% in Dr Gundry's group. We have not been required to put in a single pacemaker, compared with about 4% in their group. We do see some new bundle-branch blocks, right or left, about 10% compared with 34%, and an occasional change in various other conduction systems, but it's been very rare; 6% versus the very high percentage in their group.

Our methods are very comparable except that we do use 100 mEq of potassium in a liter of glucose rather than increasing the potassium in the electrolyte solution. This is delivered in a 4:1 dilution, four parts of blood to one part of the potassium solution, so that we end up with 20 mEq/L of potassium. We use clear prime in the pump, so that the hematocrit of the blood is down around 25%. We also use a cold pad to protect the posterior wall from the warmer blood flowing in the aorta. Our cross-clamp times, if anything, are perhaps just a little longer than those reported by Gundry and associates. Obviously there are many advantages to using the cold blood: you can use an unlimited volume, and the amount of potassium you give really is very insignificant, 50 or 60 mEq, which in the overall picture doesn't amount to very much.

I have enjoyed the presentation and the manuscript. I really think that the authors need to look past the blood cardioplegia to explain the conduction disturbances. I don't believe that's the real problem.

I would like to ask one question of Dr Gundry. I know that he has been using the retrograde coronary sinus perfusion, which seems to give a much more uniform and better myocardial cooling regardless of the status of obstruction of the coronary arteries, and I would like to know the incidence of conduction disturbances that he has seen in that particular group. I believe they have been much lower even with blood cardioplegia.

DR F. E. E. VERMEULEN (Nieuwegein, the Netherlands): I'd like to bring up some observations my colleagues and I made at the Antonius Hospital on conduction disturbances in a randomized study of 60 coronary bypass operations with five or more grafts in 1984 and 1985.

Although we did not use blood cardioplegia, we tested three fully oxygenated crystolloid cardioplegia solutions: the older St. Thomas, the Hamburg perfusion solution, and the Kirsch arresting solution followed by the Hamburg perfusion solution. The latter is based on a normal potassium but a low sodium content; in addition, the procaine and dexamethasone may afford some membrane stabilization, and 6% hydroxy ethyl starch is used for colloid-osmotic pressure.

We divided each group of 20 patients into two subgroups; 10 patients with repeat topical cooling and 10 with only initial cooling. The main differences we observed concern the frequent need for defibrillation in the St. Thomas group, and approximately 40% of patients with late postoperative dysrhythmias, sinus tachycardia, and arterial fibrillation and flutter, as well as some ventricular extopia, in the groups with St. Thomas solution. Only 2 patients showed early reperfusion conduction disturbances in each subgroup; no pacemakers were used.

In the two Hamburg protocols, however, reperfusion atrioventricular disassociation occurred in the majority of patients, with asystole followed by partial atrioventricular block and finally resulting in total, spontaneous recovery after a mean of 10, 7, 16, and 9 minutes, respectively, in the four groups (Hamburg solution with repeat cooling, Hamburg solution with only initial cooling, Kirsch and Hamburg solutions with repeat cooling, and Kirsch and Hamburg solutions with only initial cooling).

Late dysrhythmias did not occur in the subgroups with repeated cooling and occurred very rarely in those with initial cooling; no late conduction disturbances were seen and no pacemakers used.

This brings up my two questions. Dr Gundry, would you consider that different mechanisms may intervene in the reperfusion versus the late postoperative conduction disturbances? And should one not consider asystole or atrioventricular conduction block that occurs during early reperfusion but is reversible as a rather beneficial event allowing myocardial replenishing? This is different, of course, from the ominous late conduction disturbances you observed.

DR GUNDRY: I'd like to thank the discussants for their many varied and exciting comments. I was hoping we could come here to Mecca and find out what we're doing wrong, and, Dr Weisel, I appreciate your input on this. We are absolutely fascinated with the finding that topical hypothermia with ice slush may influence these conduction disturbances. I was just talking with my chairman, Dr McLaughlin, and perhaps if I had been allowed to fly to Hawaii in June I might have learned about this earlier.

Be that as it may, both our crystalloid and our blood cardioplegia patients receive ice slush. Therefore, the actual effect of the ice slush may have more to do with lowering the absolute temperature of the heart than with the effect of the blood cardioplegia. We have become interested in whether in fact we do have a real rheology problem within the heart with very cold blood, and in fact we're instituting a study now, changing our mixture in the BCD system to a 2:1, 3:1, or 4:1 ratio and comparing this with the topical hypothermia.

As to the amount of permanent pacing required, certainly we are a bit alarmed with our permanent pacing experience; however, the University of Michigan recently published their experience with blood cardioplegia. Their incidence of conduction defects were almost identical to ours, strikingly identical, including a 2% incidence of complete heart block requiring pacing. All I can assume is that compared with Toronto, where it's quite cold, life moves a little slower in Baltimore and our patients perhaps are a little slower to recover their atrioventricular node.

Dr Webb, it is true we have now been using retrograde cardioplegia. Perhaps also in answer to Dr Weisel's questions, we have found that with retrograde cardioplegia—I've not finished breaking the numbers down, but it's actually something I'm doing this month—in the first 100 consecutive patients, we have not noticed this degree of heart block with our blood cardioplegia. Again, I don't know what to attribute that to in the first place, but it may be that we are having an inadequate distribution of blood cardioplegia to the atrioventricular node when the hearts are ice cold. It's something we're going to continue to look at.

Finally, Dr Vermeulen, we have looked at arrhythmias, atrial arrhythmias as well, comparing blood and crystalloid cardioplegia. Perhaps surprisingly, there is absolutely no difference between blood and crystalloid cardioplegia in the production of atrial arrhythmias. I have used blood cardioplegia most of my life and have been convinced that the period of reversible atrioventricular block is of great benefit to the heart during the reperfusion period. I was struck, therefore, when we broke down these numbers by the fact that this period of reversible atrioventricular block in our blood cardioplegia patients very accurately predicted those patients who were going to end up with a conduction disturbance. Now, I admit that most of the conduction disturbances appear to be benign. They appear to have no effect on postoperative course, and yet I'm beginning to wonder if this reversible atrioventricular block, at least with blood cardioplegia, isn't telling us something about what's happening at the conduction system level.

Bronchogenic Carcinoma in Patients Under Age 40

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Eighty-nine patients aged 19 to 39 years were treated for bronchogenic carcinoma at Roswell Park Memorial Institute between 1973 and 1983. The male to female ratio was 1.6:1. The vast majority of patients were habitual cigarette smokers. Forty-four patients (49%) had adenocarcinoma or bronchoalveolar cell carcinoma. Twenty-seven (30%) had large cell undifferentiated carcinoma. Nine (10%) had small cell carcinoma and 6 (7%), squamous cell carcinoma. At the time of diagnosis, 2 patients (2%) had stage I disease, 3 (3%) had stage II disease, 30 (34%) had stage IIIA disease, 28 (32%) had stage IIIB disease, and 26 (29%) had stage IV disease. Only 3 patients survive. Median survival of all patients was 7.5 months. Median survival of patients whose tumor was surgically resected was 17.5 months. Advanced stage of disease at the time of diagnosis characterized this group of young patients with primary cancer of the lung. The brief duration of symptoms and the poor survival suggest this is a more aggressive tumor in younger patients than in older patients.

(Ann Thorac Surg 1989;47:391–3)

In the past, bronchogenic carcinoma was mostly a disease of elderly men. More recently, there has been a dramatic increase in the incidence of bronchogenic carcinoma among women. A small percentage of patients acquire this disease in the third or fourth decade of life or earlier. This age group, which might be expected to reflect more clearly the changing patterns of bronchogenic carcinoma, is the subject of this study.

Material and Methods

This is a retrospective study of 89 patients aged less than 40 years who were treated for bronchogenic carcinoma between 1973 and 1983 at Roswell Park Memorial Institute. During that period, 2,856 patients were treated for primary lung cancer, which makes the incidence of bronchogenic carcinoma in patients aged less than 40 years 3.1% at our institution. Patients with adenoid cystic carcinoma and carcinoid tumors were not included in this study.

The 89 patients studied had clinical staging at the time of diagnosis. Information from the medical records was used to convert staging to the newly formulated international staging system for lung cancer [1].

Complete follow-up was obtained. Only 3 patients are alive. They have survived for 74 months, 142 months, and 168 months without evidence of recurrent tumor.

Results

The age distribution of these patients was 19 to 39 years. There were 55 men and 34 women.

Increased cough, chest pain, hemoptysis, and dyspnea were the most common symptoms. Three patients whose tumors were incidental findings on routine chest roentgenograms were asymptomatic. None had undue delay of diagnosis because of equivocal roentgenograms. Duration of symptoms ranged between less than 1 month to 8 months. Average duration of symptoms was 2.4 months; median duration of symptoms was 1.5 months. The patient with the longest recorded duration of symptoms has also survived the longest. He had a Pancoast tumor, which ultimately was treated with preoperative irradiation and surgical resection.

Initial symptoms indicating advanced disease were present in 28 patients (31.5%), and included palpable lymph nodes (13 patients), pain related to bone metastases (6 patients), central nervous system symptoms related to brain metastases (5 patients), and subcutaneous nodules (4 patients).

The vast majority of the patients (76%) were habitual cigarette smokers. Smoking history was uncertain in 10. At least 43% (38/89), probably more, began smoking cigarettes as teenagers. There were 11 nonsmokers. One of the 11 nonsmokers received irradiation to the thymus during infancy. Otherwise, no etiological factors were obvious.

Tumor histology revealed a preponderance of adenocarcinomas (38 patients, 43%) and a paucity of squamous cell carcinomas (6 patients, 7%). There were 27 patients (30%) with large cell undifferentiated carcinoma, 9 (10%) with small cell carcinoma, 6 (7%) with bronchoalveolar cell carcinoma, and 2 (2%) with adenosquamous cell carcinoma. One patient had a carcinosarcoma. The 11 patients who were nonsmokers had predominantly adenocarcinoma (7 patients). The remaining 4 nonsmokers had bronchoalveolar cell carcinoma, large cell carcinoma, small cell carcinoma, and carcinosarcoma.

Ninety-four percent (84) of the patients had stage III or stage IV disease at the time of diagnosis: stage I, 2 patients; stage II, 3; stage IIIA, 30; stage IIIB, 28; and stage IV, 26.

Thirty patients (34%) underwent an exploratory thora-

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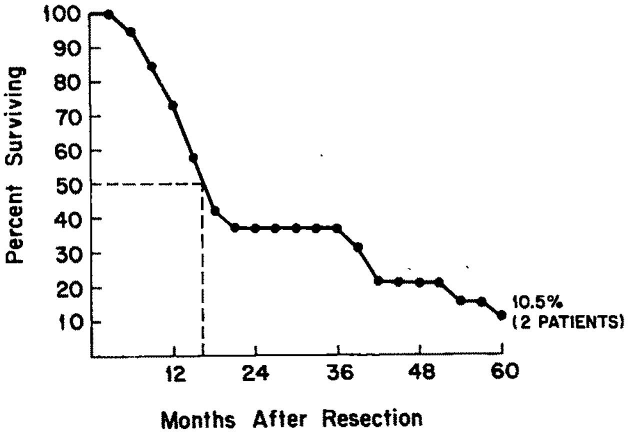

Fig 1. Survival curve for 19 patients who had surgical resection. Broken lines indicate median survival.

cotomy. Of these patients, 19 (21%) had surgical resection (ten lobectomies, six pneumonectomies, and three wedge resections). There were no intraoperative deaths among the patients treated with surgical resection. One patient who had an exploratory thoracotomy died of a pulmonary embolus on the day after operation. The survival curve of the patients having resection is shown in Figure 1.

Patients who had unresectable disease were treated with palliative radiation therapy, chemotherapy, immunotherapy, or combinations of each. Several received only symptomatic care.

The survival curve of the entire group is shown in Figure 2. There was no significant difference in survival according to sex or cell type.

Comment

Cigarette smoking apparently is an important causative factor in the development of cancer of the lung even in this younger age group. Forty-three percent of our patients (38/89) were habitual cigarette smokers as teenagers. An accurate smoking history was not obtained for all patients. It is likely that a majority were addicted to cigarettes as teenagers. Three previously published series [2–4] of patients of the same age group with primary lung cancer have a combined 90% incidence of cigarette smokers (155/172).

The male to female ratio of 1.6:1 in our group of patients probably reflects the increased use of cigarettes by teenage girls. The male to female ratio of patients with bronchogenic carcinoma older than 40 years during this same period was 2.4:1 at our institution. This difference is significant ($p = < 0.005$; $\chi^2 = 58.2$).

The high incidence of adenocarcinoma and paucity of younger patients with squamous cell carcinoma is similar to findings in other published series [2–6]. This suggests that squamous cell carcinoma requires a longer exposure to carcinogens and, consequently, occurs less frequently in the young. McKneally [7] concluded that the scarcity of the more readily curable squamous cell carcinoma, rather than an altered biology of the host, accounts for the poor prognosis for these patients.

The high incidence of advanced stage of disease at diagnosis in these younger patients is another finding commonly reported [2–6]. In our patients, even the 5 with stage I and stage II disease did poorly. The tumor was resected by lobectomy in all 5. Four received adjuvant irradiation or chemotherapy, or both. They survived from 5 to 53 months, but all 5 died of recurrent cancer.

The 3 asymptomatic patients in whom the tumors were found incidentally on routine roentgenograms underwent surgical resection of the tumor by lobectomy. However, lymph node metastasis was present in all 3 (2, hilar, and 1, subcarinal). Although these patients survived for 18, 38, and 53 months, each died of recurrent tumor.

Only 3 patients survive. One had limited small cell carcinoma, which was diagnosed in 1974. She was treated with chemotherapy (Cytoxan [cyclophosphamide], hexamethylmelamine, and Adriamycin [doxorubicin hydrochloride] alternating with nitrogen mustard, vinblastine sulfate, and procarbazine hydrochloride), radiation therapy, and immunotherapy (bacille Calmette-Guérin), and survives without evidence of disease. The pathology slides were recently reviewed by another group of pathologists, and the diagnosis of small cell carcinoma was confirmed.

Another survivor had "palliative" wedge resection of an adenocarcinoma 6 years ago at another hospital. After two courses of chemotherapy, a repeat thoracotomy was done, and paratracheal lymph nodes including a 3 × 3-cm mass containing adenocarcinoma were resected. This was followed by radiation therapy and more chemotherapy. At last contact, the patient had no evidence of recurrent disease 74 months after operation.

The other surviving patient had a Pancoast tumor (large cell undifferentiated), which was resected after radiation therapy. There was no lymph node involvement. He remains alive without recurrence more than 10 years after craniotomy and radiation therapy for a solitary brain metastasis. As previously mentioned, this patient had the longest duration of symptoms (8 months) before diagnosis and has survived the longest after surgical resection.

This study demonstrated (1) that the male to female ratio is significantly smaller in younger patients with bronchogenic carcinoma, (2) that a history of heavy ciga-

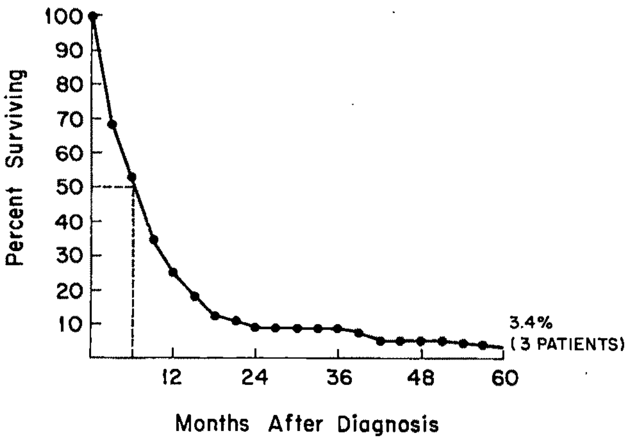

Fig 2. Survival curve for entire group of 89 patients. Broken lines indicate median survival.

rette use at an early age is frequently obtained, and (3) that long-term survival and cure of bronchogenic carcinoma in younger patients is very uncommon. Advanced stage of disease at the time of diagnosis characterized this group of young patients with primary cancer of the lung. The relatively brief duration of symptoms and the dismal survival suggest that bronchogenic carcinoma is a more aggressive tumor in younger patients than in older patients.

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Mucoepidermoid Lung Tumors

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Mucoepidermoid lung tumors are uncommon, representing 0.2% of all lung tumors and 1% to 5% of bronchial adenomas. Eighteen patients with mucoepidermoid tumors are reported. There were 10 male and 8 female patients with a mean age of 36.8 years (range, 9 to 62 years). On the basis of mitotic activity, cellular necrosis, and nuclear pleomorphism, we subclassified these tumors as low grade (15 patients) or high grade (3 patients). The achievement of complete resection and low-grade versus high-grade staging correlated with prognosis. All 12 patients who had a low-grade tumor that was completely excised are alive with no evidence of disease at a mean follow-up of 4.7 years (range, 1 to 27 years). All high-grade tumors proved fatal within 16 months. Two of the 3 high-grade tumors were unresectable because of extensive local disease. Patients with low-grade tumors and microscopically positive margins require close follow-up and can undergo a successful repeat resection. Nine of the 16 resections were sleeve resections, highlighting the importance of conservative lung-sparing procedures in these central airway tumors. Both patients with an unresectable high-grade tumor had radiation therapy postoperatively and died 11 months later. The role of radiation therapy with high-grade tumors or incomplete resection has yet to be determined.

(Ann Thorac Surg 1989;47:394–9)

Mucoepidermoid tumors of the trachea and bronchi are uncommon tumors, which historically have been included under the term *bronchial adenoma*. These tumors were described within the bronchi in 1952 by Smetana and co-workers [1] and Liebow [2]. Their infrequent occurrence and wide spectrum of clinical aggressiveness have resulted in controversy as to whether they are benign or malignant tumors. The first review of mucoepidermoid tumors from the Massachusetts General Hospital was in 1958 [3], when 5 patients were reported and the benign nature of the tumors was emphasized.

Material and Methods

Clinical records and pathological material were reviewed for 18 patients. Fourteen of the patients were treated at the Massachusetts General Hospital from 1948 to the present. The 5 patients with mucoepidermoid tumors first reported from this institution by Sniffer and colleagues [3] are included in this review. Four were patients whose slides were seen in consultation by one of us (E.J.M.).

Slides stained with hematoxylin and eosin were available and reviewed in each case. Histochemical stains were used on all specimens from the patients seen at the Massachusetts General Hospital. Electron microscopic examination was used in 3 cases.

Clinical Features

There were 10 male and 8 female patients with a mean age of 36.8 years (Table 1). Only 4 of the 18 were known smokers. Presenting symptoms could be divided into three groups: bronchial irritation, bronchial obstruction, and constitutional symptoms. Symptoms of bronchial irritation were most common and included cough, hemoptysis, and wheezing. Four patients had postobstruction pneumonia when first seen. Constitutional symptoms including weight loss and pain were indicative of a more aggressive tumor. Five patients were asymptomatic; their tumors were identified on routine chest roentgenograms. Fifteen patients were free of metastatic disease at the time of operation. One patient had an intrapulmonary metastasis resected at the time of operation, and 2 patients had unresectable tumors.

Thirteen of 18 admission chest roentgenograms were abnormal. The most common abnormality was the tumor nodule itself, followed by postobstruction pneumonia or atelectasis. Five roentgenograms were interpreted as normal; 4 of the patients had a central tracheal tumor, and 1 had a small tumor involving the origin of the superior segmental bronchus of the left lower lobe.

Bronchoscopic biopsies were performed in 8 patients.

Pathological Findings

The resected tumors ranged in maximum cross-sectional area from 0.6 to 5.5 cm. All resected tumors were exophytic and noncystic. Eleven tumors were confined to the mucosa of the trachea or bronchi or to the internal perichondrium (Figs 1, 2), but 3 had invaded between cartilage plates to the external perichondrium, and 4 had invaded into surrounding adventitia or lung parenchyma.

Lymph node specimens from 12 patients were available for histological examination. Two had lymph node involvement, 1 by direct invasion into carinal and hilar nodes and the other by invasion of the peribronchial nodes. In 6 patients, no lymph nodes were included in the surgical specimens. One patient had perineural invasion by tumor. No other lymphatic or vascular invasion was found. The biggest tumor, which involved both the tra-

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Table 1. Clinical Features

Variable	Result
Age (yr)	36.8 (range, 9–62)
Sex (M:F)	10:8
Smoker	4/16 (2 unknown)
Presenting symptoms[a]	Cough Hemoptysis Pneumonia Weight loss Asymptomatic
Chest roentgenographic findings[a]	Nodule Infiltration Normal (5/18)
Bronchoscopic diagnosis	100% positive

[a] These are listed in order of frequency.

chea and the bronchus, produced a single metastasis in the lung distant from the primary tumor. Bronchial obstruction manifested by mucous plugs, organizing pneumonia, or bronchiectasis was present in 6 of 8 patients in whom lung parenchyma was examined.

All tumors had a mixture of cell types, including squamous, intermediate, or mucous cells. Fourteen of the 18 tumors were composed mainly of squamous or intermediate cells, 2 were composed mainly of glandular or mucous cells, and 2 showed a roughly equal admixture of squamous or intermediate and mucous or glandular cells. The mitotic activity of the tumors ranged from none detectable to 20 mitoses per ten high-power fields. Eleven had no mitoses, 5 had one per ten high-power fields, 1 had five per ten high-power fields, and 1 had 20 per ten high-power fields. Eleven tumors had no necrosis, 5 had necrosis of individual cells, and 2 had necrosis of small or large groups of cells.

Nuclear pleomorphism was evaluated in terms of degree of hyperchromatism, clumping of chromatin, and enlargement of nucleoli. Seven tumors had slight nuclear pleomorphism, 8 had moderate nuclear pleomorphism, and 3 had marked nuclear pleomorphism. Those with marked nuclear pleomorphism were also the tumors that had the more extensive mitotic activity and necrosis. No correlation between tumor grade and proportion of mucous or squamous cells was found.

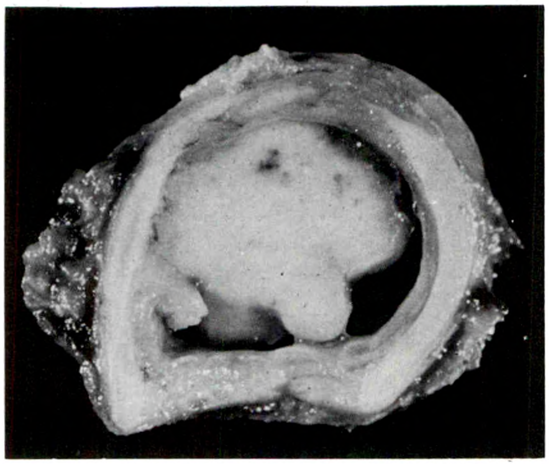

Fig 1. Cross section of trachea with solid white tumor filling lumen and infiltrating mucosa (9 to 12-o'clock position).

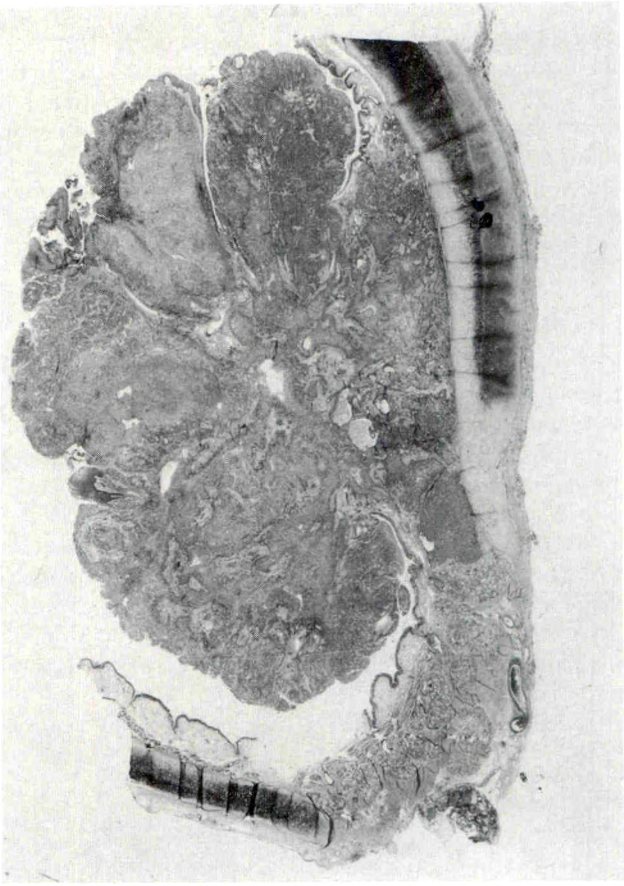

Fig 2. Mucoepidermoid tumor arising in tracheal mucosa (right) and forming a solid intraluminal mass (whole mount). (Hematoxylin and eosin, ×5.)

On the basis of mitotic activity, cellular necrosis, and primarily nuclear pleomorphism, we subclassified these tumors as low grade (15 patients) or high grade (3 patients) (Figs 3–6). A further breakdown of low-grade tumors into low and intermediate varieties proved less clear and without correlation with clinical outcome. Low-grade versus high-grade staging, as will be shown, correlated with operative assessment of tumor aggressiveness and with prognosis.

Treatment

All 18 patients were explored. When possible, conservative, lung-sparing procedures were utilized. Operative procedures included three tracheal resections with primary reconstruction, five lobectomies, two bilobectomies, five sleeve resections, and one sleeve right pneumonectomy with en bloc resection of positive mediastinal lymph nodes (Table 2). Two tumors were unresectable because of extensive local invasion. Both of these patients received radiation therapy postoperatively. No other therapy was administered.

A young female patient underwent a complicated tracheal resection for a subglottic low-grade mucoepidermoid tumor. The proximal resection margin was microscopically positive. Further resection would have required a laryngectomy, and in view of the low-grade nature of the tumor, it was elected to follow her.

One patient who underwent a right upper lobectomy had a local recurrence 9 years later. A sleeve resection of the bronchus was successful.

Results

There were no operative deaths. Twelve patients had a complete resection both clinically and pathologically (Fig 7). All of them had low-grade mucoepidermoid tumors. All patients from this group are alive without evidence of recurrence at a mean follow-up of 4.7 years (range, 1 to 27 years).

Six patients had an incomplete resection; 2 of them had unresectable tumors. One patient with a high-grade mucoepidermoid tumor underwent a sleeve pneumonectomy but had extensive hilar and mediastinal lymph node involvement. This patient received no adjuvant therapy and died 16 months postoperatively.

Three patients were left with microscopically positive bronchial margins. All of them had tumors classified as low grade. One patient had recurrence clinically 9 years later and underwent a complete repeat resection. Another patient had a left lower lobectomy 6 months ago; there are no plans for further resection. The third patient had a positive margin determined intraoperatively, but this was accepted because a laryngectomy would have been required. No definite plans for radiation therapy for these last 2 patients have been made.

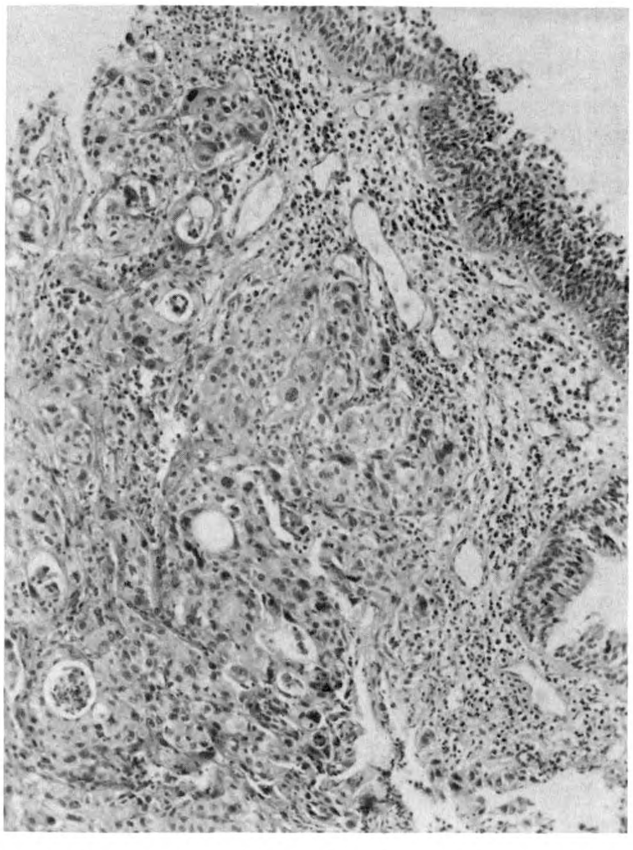

Fig 3. Photomicrograph of low-grade mucoepidermoid tumor. A solid nest of tumor (bottom) has epidermoid characteristics with occasional mucin-filled vacuoles. Overlying respiratory mucosa (top) is inflamed and edematous but intact. (Hematoxylin and eosin, ×125 before 3% reduction.)

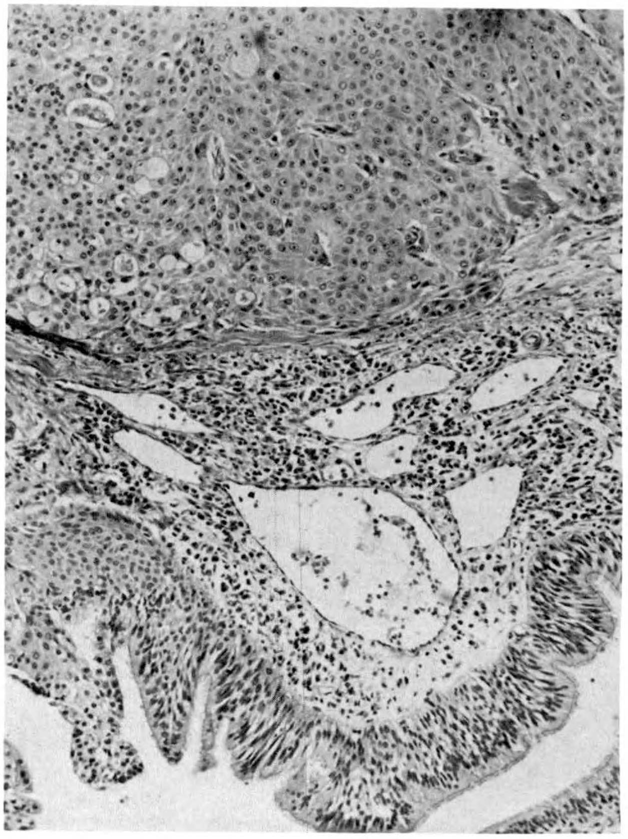

Fig 4. Photomicrograph of high-grade mucoepidermoid tumor. The tumor irregularly infiltrates the surrounding tissue. Some nuclei are large and pleomorphic. (Hematoxylin and eosin, ×125 before 3% reduction.)

Two patients had a high-grade tumor that was unresectable. Both patients died 11 months postoperatively despite radiation therapy.

Comment

The tracheal and bronchial upper airway submucosa and the salivary glands contain serous and mucous glands that are histologically similar [4, 5]. Tumors arising from these glands, regardless of the location, share similar histology and biological activity. These tumors include adenoid cystic carcinoma, mucoepidermoid tumor, mixed (pleomorphic) adenoma, and oxyphil adenoma.

Mucoepidermoid tumors are uncommon, constituting approximately 0.2% of all lung tumors and 1% to 5% of tumors included under the term *bronchial adenoma*. They can occur over a broad age range, which includes children

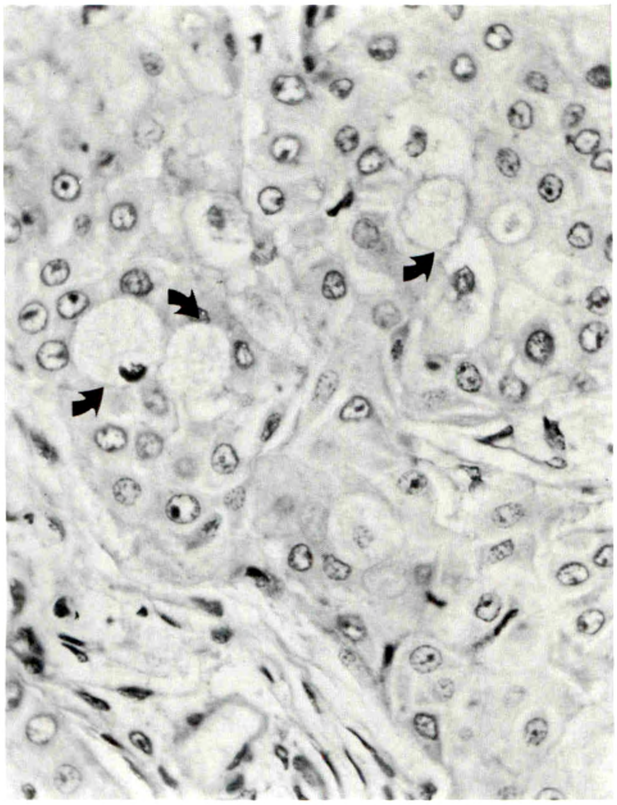

Fig 5. Photomicrograph of low-grade mucoepidermoid tumor. Epidermoid cells have distinct cytoplasmic membranes and intercellular bridges. Several cells have mucous vacuoles (arrows). *(Hematoxylin and eosin, ×500 before 3% reduction.)*

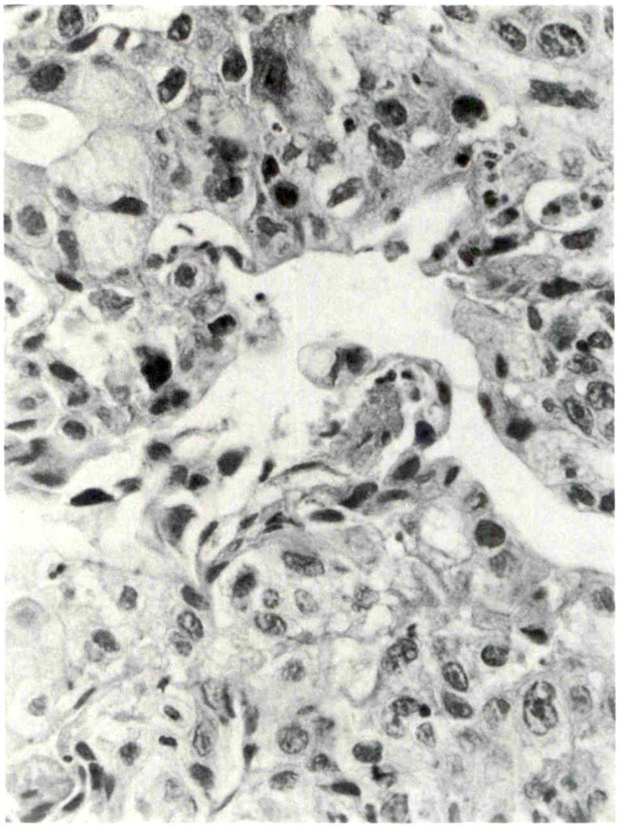

Fig 6. Photomicrograph of high-grade mucoepidermoid tumor. Large nuclei have prominent nucleoli. Individual necrotic tumor cells are present. (Hematoxylin and eosin, ×500 before 5% reduction.)

[6–10]. The mean age in our series, 36.8 years, is considerably younger than in most series, but our series demonstrates the usual broad spread in age (range, 9 to 62 years). Although some have reported a male predominance, most reports, including our own, fail to demonstrate a clear predilection based on sex. Smoking is not a major risk factor. Symptoms are primarily those of bronchial irritation and obstruction, and include cough, wheezing, hemoptysis, and postobstruction pneumonia. The more worrisome constitutional symptoms of pain, weight loss, and malaise, which were common in the series of Turnbull and colleagues [11], reflect the aggressive potential of these tumors.

A chest roentgenogram will usually show either the tumor or postobstruction changes. However, in our study, five of 18 chest roentgenograms were interpreted as normal because of the central location of the tumors. Although a diagnosis can be obtained by sputum cytology, this is unnecessary as tumors can be visualized and bronchoscopic biopsies can be done successfully. Others have confirmed the safety of bronchoscopic biopsy of mucoepidermoid tumors; such biopsies can be done without resulting in bleeding complications.

Our concept of mucoepidermoid tumors, which is in the context of the current understanding of carcinomas of the lung in general, is that the tumor arises from a single cell type but is differentiated primarily along either squamous or glandular lines, or both. In this sense, it is not surprising that there is a spectrum of cytoplasmic differentiation. The minimum features that we require for a diagnosis of tracheobronchial mucoepidermoid tumor are as follows: (1) origin within a conducting airway that contains cartilage; (2) presence of squamous or intermediate elements that are manifested by either intercellular bridges or cytoplasmic membranes; and (3) presence of glandular elements that are manifested either by individual mucous cells, glandular cells, or signet ring cells.

We believe that mucoepidermoid tumors and adenosquamous carcinomas are the same entity, with the term

Table 2. Operative Procedures

Procedure	No. of Patients
Tracheal resection and reconstruction	3
Lobectomy	5
Bilobectomy	2
Sleeve resection	5
Sleeve pneumonectomy	1
None	2[a]

[a] These 2 patients had unresectable tumors.

mucoepidermoid tumor used for tumors arising in cartilage-containing bronchi and the term *adenosquamous carcinoma* used for tumors arising in the periphery of the lung beyond a grossly recognizable bronchus. Mucoepidermoid tumors in the central airways can be of either low-grade or high-grade malignancy, whereas adenosquamous carcinomas, which arise in the periphery, are virtually always high-grade tumors.

Whether these tumors are benign or malignant is an issue that has been argued since they were described in 1952. In 1958, Sniffer and associates [3] presented 5 patients with mucoepidermoid tumors, and concluded that these tumors were slow-growing, benign neoplasms similar in their biological activity to carcinoid tumors. Later Wilkins and co-workers [12] reported that bronchial adenomas in general (including mucoepidermoid tumors) were tumors of low-grade malignancy, which were amenable to conservative surgical excision. After excision, long-term survival could be expected. Many other authors [11, 13–15], however, have emphasized the malignancy of both bronchial mucoepidermoid tumors and bronchial adenomas. Leonardi and associates [16] reviewed the cases of 7 patients with mucoepidermoid tumors. Six patients had low-grade benign tumors, and 1 patient had a high-grade malignant form, which proved fatal despite radiation therapy. Leonardi and associates concluded that mucoepidermoid tumors are capable of a spectrum of biological activity.

Recently, Yousem and Hochholzer [17] reviewed 58 cases of mucoepidermoid lung tumors and correlated pathological grading (low versus high grade) with clinical course. As with our series, cytological features used to distinguish low grading versus high grading included cellular atypia (nucleomegaly, pleomorphism, and mitotic activity) and tumor necrosis. All patients with low-grade tumors for whom follow-up information was obtained were either alive with no evidence of disease or had died of unrelated causes (mean follow-up, 67 months). Those with high-grade tumors were older (44.5 years versus 34.8 years) and had a 4-year survival of 66%. In that series, the worst prognostic pathological feature was hilar lymph node metastasis.

Our experience demonstrates that mucoepidermoid tumors can be divided into low grade and high grade on the basis of histological criteria. Staging is predictive of clinical tumor aggressiveness and prognosis. The most important factors in the prognosis include histological grading and the ability to achieve a complete surgical resection (see Fig 7). These are the same prognostic factors found in the management of mucoepidermoid tumors of salivary gland origin [18].

The majority (12) of tumors in our series were low grade, localized or locally invasive, and amenable to complete surgical resection with the expectation of cure. All patients in this group are alive without evidence of disease at a mean follow-up of 4.7 years. Three patients had high-grade tumors, 2 of which were unresectable because of extensive local invasion. The mean age of these patients was 40 years (32, 34, and 54 years), close to the mean age for the entire group. This suggests that neither extreme of age predisposes to the high-grade variety of tumor. In all 3 patients, the high-grade tumors proved fatal within 16 months. No patient had documented distal metastasis preoperatively; however, 1 patient had cerebral metastasis noted at postmortem examination.

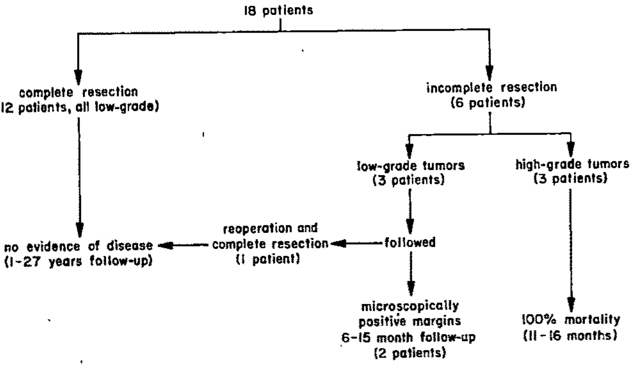

Fig 7. *Results of treatment.*

It is the third group (see Fig 7), those patients with low-grade tumors who have microscopically positive margins after resection, who deserve special mention. In our series, this group comprised 3 patients. One patient had a local recurrence 9 years after a right upper lobectomy and was successfully treated by sleeve resection. Another patient, a 9-year-old girl, had microscopically positive margins after a left lower lobectomy 6 months ago (review of slides only). The third patient (15 months after operation) had a low-grade subglottic mucoepidermoid tumor with microscopically positive margins noted at operation. Further resection would have required a laryngectomy, and it was therefore elected to follow her. The outcome of patients in this group is unresolved. Whether clinically significant recurrences, metastasis, or degeneration to high-grade staging will develop is unclear. None of these 3 patients have received radiation treatment, and its efficacy in treating such patients is unproven. Nonetheless, the importance of close follow-up must be strongly emphasized. When recurrences are identified bronchoscopically, reoperation and resection have been successful.

The proximal location of these tumors, the prevalence of the low-grade variant (15/18 in our series), and the infrequency of hilar and mediastinal lymph node involvement (2/12 in our series) make these tumors particularly amenable to conservative resection. In a series of 67 mucoepidermoid tumors cited by Breyer and associates [19], only 3 tumors were located distal to a lobar bronchus. Ten of the tumors in our series involved the trachea or mainstem bronchi, 4 involved lobar bronchi, and 4 involved segmental bronchi. There was no side predominance (7 right, 6 left, 5 central). The high incidence of tracheal involvement reflects our referral pattern and experience with tracheal surgery. In addition, however, there were three sleeve lobectomies, one sleeve right pneumonectomy, and five sleeve resections of the left mainstem bronchus and bronchus intermedius, for a total of nine of 16 resections.

Radiation therapy is often considered in patients who undergo an incomplete resection or have unresectable tumors. However, data to support its use are lacking. In our series, 2 patients with unresectable high-grade mucoepidermoid tumors were given irradiation postoperatively. Both died of the disease 11 months later.

Conclusions

Mucoepidermoid tumors are uncommon tumors that can occur over a wide age range. They usually are seen early in their course, and the diagnosis can be made bronchoscopically. Pathological staging of these tumors is essential, and two forms, a low grade and a high grade, have been identified. Prognosis is dependent on staging, assessment of clinical aggressiveness at operation, and the achievement of negative surgical margins. Neither the older nor the younger age group was predisposed to high-grade tumors. Preoperatively, unless there is documented metastasis or clear unresectable local invasion, operative resection is recommended. The central airway location of these tumors makes them especially amenable to conservative resection.

The outcome for patients with low-grade mucoepidermoid tumors with microscopically positive margins is unresolved, but all require close follow-up. The role of radiotherapy in these patients or in patients with high-grade tumors has yet to be determined.

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Apparent Coagulopathy Caused by Infusion of Shed Mediastinal Blood and Its Prevention by Washing of the Infusate

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We found that reinfusion of shed mediastinal blood (SMB) after a cardiac operation was associated with laboratory evidence of disseminated intravascular coagulation. In view of this, we compared the effect of infusing washed or unwashed SMB on the coagulation profiles and blood use of two serial groups of patients undergoing cardiopulmonary bypass. We found that the results of testing for fibrin degradation products converted from negative to positive in 17 of 20 patients who received unwashed SMB versus 1 of 14 patients who received washed SMB ($p < 0.0001$). Other coagulation studies did not reveal disseminated intravascular coagulation in either group, nor were there differences in blood use between the two groups. The unwashed SMB contained high titers of fibrin degradation products (mean reciprocal titer = 354 ± 161) compared with washed SMB (mean reciprocal titer = 34 ± 18) ($p < 0.01$). Based on the volume of SMB infused, the amount of fibrin degradation products in unwashed SMB was sufficient to account for the positive fibrin degradation product assays after infusion in this group. We conclude that infusion of unwashed SMB may confuse the interpretation of tests for disseminated intravascular coagulation or fibrinolysis. As this could lead to unnecessary blood component use and is preventable by washing before infusion, we recommend that the routine infusion of unwashed SMB no longer be employed.

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Homologous blood transfusion therapy entails substantial risks, including transfusion reactions, alloimmunization, and transmission of diseases such as hepatitis, cytomegalovirus, and acquired immunodeficiency syndrome due to human immunodeficiency virus.

Cardiac surgical patients comprise a high-risk group in that they often require transfusion during hospitalization. Schaff and colleagues [1] reported an average homologous blood usage of 8.4 units per adult patient undergoing coronary artery bypass grafting in 1976. Since that time, autologous transfusion techniques, which include perioperative phlebotomy with hemodilution, salvaging of intraoperative blood loss by cell washers, and postoperative autotransfusion of shed mediastinal blood (SMB), have reduced transfusion requirements by 26% to 50% [2, 3].

Early reports [4, 5] on the reinfusion of SMB warned of coagulopathies, but others [6] have demonstrated no adverse effects on the control of hemostasis. At our institution, evaluation of several patients who received SMB in the postoperative period revealed several in whom abnormal coagulation profiles developed. The association between the apparent coagulopathy and the administration of SMB stimulated us to investigate the effects of this product on the coagulation system and to ascertain if the coagulopathy could be prevented by washing the SMB before reinfusion.

Material and Methods

Two nonrandomized groups of patients were studied serially during the 17-month period between April 1985 and September 1986. Group 1 (unwashed SMB group) included 21 patients who received unmodified SMB collected by means of the Sorenson drainage system (Sorenson Research Corp, Salt Lake City, UT) with reinfusion through a 40-μm blood filter without further processing. Group 2 (washed infusate group) included 17 patients who similarly had the SMB collected through the Sorenson drainage system, but before reinfusion, the SMB was washed in a Haemonetics Cell Saver model CSII (Haemonetics Corp, Braintree, MA) using 1,000 mL of normal saline solution.

The data base included the operation performed, the length of cardiopulmonary bypass (CPB), the total chest tube output at 24 hours, average hourly chest tube output before and after reinfusion of unwashed or washed SMB, and the volume of shed blood infused. Hematological data included blood count, prothrombin time (PT), activated partial thromboplastin time (PTT), platelet count, fibrinogen level, protamine paracoagulation phenomenon, and analysis for fibrin degradation products (FDP). The FDP were measured by the Thrombo-Wellco latex agglutination method (Burroughs Wellcome Co, Research Triangle Park, NC), which has a sensitivity of 2 μg/mL for

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Table 1. Comparison of Patient Groups

Variable	Group 1 (Unwashed SMB) (n = 21)	Group 2 (Washed SMB) (n = 17)
Age (yr)	60 ± 7	63 ± 5
Operation		
CABG	17	11
Valve replacement	3	4
Valve replacement − CABG	0	1
Reoperation for CAD	1	1
No. of vessels bypassed/patient	4.5 ± 2.2	4.7 ± 1.1
Preoperative hematocrit (%)	42 ± 3	41 ± 5
CPB time (min)	94 ± 38	128 ± 34[a]
Chest tube drainage (total/24 h)	1,037 ± 357	1,380 ± 828

[a] Significance: $p < 0.005$ compared with group 1.

CABG = coronary artery bypass grafting; CAD = coronary artery disease; CPB = cardiopulmonary bypass; SMB = shed mediastinal blood.

FDP, chiefly the D and E fragments [7]. As normal serum values of FDP are less than 10 μg/mL, normal serum diluted 1:5 gives a negative result. The patients' sera were tested at two standard dilutions of 1:5 and 1:20, and the results were reported as either positive or negative at these concentrations.

These data were collected on the patient's arrival in the surgical intensive care unit and again one half hour after infusion of either unwashed or washed SMB. Patients were not transfused with other blood products between blood sampling before and after infusion of SMB. Blood counts were also obtained preoperatively and 24 hours postoperatively. The hematological analyses were performed in the Veterans Administration Medical Center Department of Laboratory Services using standard techniques. Samples of the unwashed or washed SMB were obtained before infusion into the patients, and were analyzed for hematocrit, free hemoglobin, and the titer of FDP. For ease of interpretation of the FDP assay, the reciprocal of the highest dilution (titer) giving a positive result is reported. Total blood product usage was tallied for the entire hospital stay.

Mathematical analysis employed unpaired *t* testing except for comparisons between the preinfusion and postinfusion data sets of patients who received either unwashed or washed products, in which case the paired *t* test was used. McNemar's test for matched pairs with a dichotomous outcome was utilized for the FDP assays, and significant differences were assumed to exist when the probability of a random occurrence was less than 5% ($p < 0.05$). Data in the tables are presented as the mean ± one standard deviation unless otherwise stated.

Results

As shown in Table 1, there were no differences between the two patient groups with respect to age, type of operation, or preoperative hematocrit. On the other hand, the duration of CPB was significantly longer in the group subsequently given washed SMB (group 2). There was no correlation between the duration of CPB and the clinical evaluation of bleeding, and the two groups had similar amounts of total chest tube drainage after operation.

A mean volume of 405 ± 130 mL of SMB was collected from and given to the group that received unwashed SMB (group 1) and a mean volume of 537 ± 173 mL of SMB was collected in group 2 ($p < 0.01$ versus group 1). After processing, a mean of 240 ± 50 mL of washed SMB was given. The physical characteristics of unwashed and washed SMB are shown in Table 2. The SMB did not clot in any of the samples, and a small subset was tested to confirm nonclotting PT and PTT assays (n = 3 each), low fibrinogen levels (less than 50 mg/dL; n = 3), and decreased factor VIII levels (17.5% ± 1%; n = 4). The platelet count was also low (37,000 ± 21,000 mL; n = 6). The entire series was not tested because results are well described in the literature [3, 6], our data correspond well to the previously reported results, and the focus of our study was on other factors.

As expected, the hematocrit of the washed infusate was higher than that of the unwashed SMB because of red cell concentration during the washing process. In addition, both the free hemoglobin level and titer of FDP were significantly lower in washed SMB (see Table 2). Extended serum dilutions were performed to ascertain the concentration of FDP in the unwashed infusate. The FDP assays were positive in SMB at reciprocal titers of 354 ± 161 (median titer = 300). These values were significantly reduced to 34 ± 18 (median titer = 40) by washing.

The effects of an operation with CPB and infusion of unwashed versus washed SMB on chest tube drainage and laboratory tests of hemostasis are shown in Table 3. No significant difference was observed between the preoperative and postoperative values of hematocrit between the two groups or in the amount of chest tube drainage before or after infusion of SMB. There were also no significant differences between groups for initial values of PT, PTT, platelets, or fibrinogen measured on arrival in the intensive care unit. After infusion of unwashed SMB, however, there was a significant decrease in PT compared with the corresponding value before infusion ($p < 0.001$).

Table 2. Comparison of Unwashed and Washed Shed Mediastinal Blood

Variable	Group 1 (Unwashed SMB)	Group 2 (Washed SMB)
Hematocrit (%)	25 ± 9	39 ± 15[a]
Free hemoglobin (mg/100 mL)	298 ± 164	112 ± 77[a]
FDP titer[b]	354 ± 161	34 ± 18[a]
Volume SMB processed (mL)	405 ± 130	537 ± 173[a]
Volume SMB infused (mL)	405 ± 130	240 ± 50

[a] Significance: $p < 0.01$ compared with group 1. [b] The FDP titer was the reciprocal value of highest dilution of sample resulting in a positive test for FDP (see Material and Methods).

FDP = fibrin degradation products; SMB = shed mediastinal blood.

Table 3. Comparison of Hematological and Hemostatic Data Before and After Infusion of Unwashed and Washed Shed Mediastinal Blood

	Group 1 (Unwashed SMB)		Group 2 (Washed SMB)	
Variable	Before	After	Before	After
Chest tube output (mL/h)	159 ± 59	43 ± 20	203 ± 100	62 ± 49
Hematocrit (%)	42 ± 3	27 ± 4	41 ± 5	27 ± 4
Platelets (× $10^5/\mu L$)	122 ± 38	110 ± 33	126 ± 54	118 ± 42
PT (ratio)[a]	1.23 ± 0.07	1.13 ± 0.11[b]	1.23 ± 0.12	1.21 ± 0.16
PTT (ratio)[a]	1.22 ± 0.19	1.30 ± 0.35	1.30 ± 0.40	1.48 ± 0.53
Fibrinogen (mg/dL)	183 ± 43	195 ± 67	205 ± 64	217 ± 84
Protamine paracoagulation phenomenon[c]	0/20	2/20	0/14	0/14
FDP[c]	2/20	19/20[d]	5/14	5/14

[a] This ratio is expressed as the ratio of the patient's value over the control value. [b] Significance: $p < 0.001$ compared with value obtained before infusion. [c] Data are reported as the number of patients testing positive over the total number tested. [d] Significance: $p < 0.0001$ compared with value obtained before infusion.

FDP = fibrin degradation products; PT = prothrombin time; PTT = activated partial thromboplastin time; SMB = shed mediastinal blood.

Complete preinfusion and postinfusion data on FDP were available for 20 of the 21 patients in group 1 (unwashed SMB) and 14 of the 17 in group 2 (washed SMB) (see Table 3). In group 1, 2 of 20 patients had positive FDP tests before infusion of SMB (both were positive only at 1:5 dilutions). As shown in Figure 1A, after infusion of unwashed SMB, 19 of 20 patients either had increases in FDP titer or converted from negative to positive FDP assays (10 of the patients with a previously negative assay had a positive assay at 1:5 dilution, 7 had a positive assay at 1:20 dilution, and the 2 who had a positive assay at 1:5 dilution converted to a positive assay at 1:20). Thus, in only 1 patient who received unwashed SMB did the assay remain negative for FDP. In comparison, 5 of 14 patients in group 2 had positive tests for FDP (at 1:5 dilution) before infusion. After the washed product was infused, only 1 patient whose assay was previously negative had a positive result (at a 1:5 dilution only), and 1 patient whose assay was positive for FDP before infusion converted to a negative FDP assay (Fig 1B). Analysis using McNemar's test revealed a highly significant difference ($\chi^2 = 15.06$, $p < 0.0001$) between the preinfusion and postinfusion results of tests for FDP in group 1 but not group 2 ($\chi^2 = 0.50$, $p < 0.48$).

Table 4 shows predicted FDP assay results after autotransfusion of either unwashed or washed SMB in a hypothetical man weighing 70 kg. Infusion of unwashed SMB at a mean collection volume of 405 mL with an FDP titer positive at a mean serum dilution of 1:354 would give positive results in the FDP assay at both 1:5 and 1:20 test dilutions. In contrast, infusion of a mean volume of 240 mL of washed SMB would not be expected to give rise to a positive test for FDP.

Blood product administration is listed in Table 5. There were no significant differences between groups in the transfusion of packed red cells, fresh frozen plasma, or platelets. In the group receiving the washed infusate, 2 patients had preoperative hematocrits of 33% and 34%; these patients received 5 of the 17 units of blood used postoperatively. In the unwashed infusate group, only 1 patient had a preoperative hematocrit of 34%, and he received 2 of the 8 units of packed red blood cells in the postoperative period. The mean red cell usage for the combined groups was 0.7 unit per patient. Fresh frozen plasma was used in 4 patients in each group (mean, 0.5 unit per patient overall). Platelets were utilized in no patients and 3 patients receiving unwashed and washed SMB, respectively (mean, 0.5 unit per patient). Transfusion was avoided entirely in 26 (68%) of the 38 patients.

Comment

Autotransfusion grew from the need to have a ready source of blood for infusion into rapidly hemorrhaging

Table 4. Predicted Fibrin Degradation Product Assay Results After Autotransfusion of Shed Mediastinal Blood[a]

Variable	Group 1 (Unwashed SMB)	Group 2 (Washed SMB)
Volume infused (mL)	405	240
FDP titer (reciprocal)	354	34
Total FDP infused (μg)	286,700	16,300
Plasma volume (mL)	3,800	3,800
Predicted FDP (μg/mL)	75	4.3
Predicted FDP in assay[b]		
1:5 Serum dilution	15 (+)	0.8 (−)
1:20 Serum dilution	3.7 (+)	0.2 (−)

[a] The model for this table was a patient weighing 70 kg with a postoperative hematocrit of 27%. [b] Numbers are predicted FDP in micrograms per milliliter after indicated serum dilution for FDP assay. Signs in parentheses are expected results of FDP assay with associated concentration of FDP. The FDP assay has a sensitivity of 2 μg/mL.

FDP = fibrin degradation products; SMB = shed mediastinal blood.

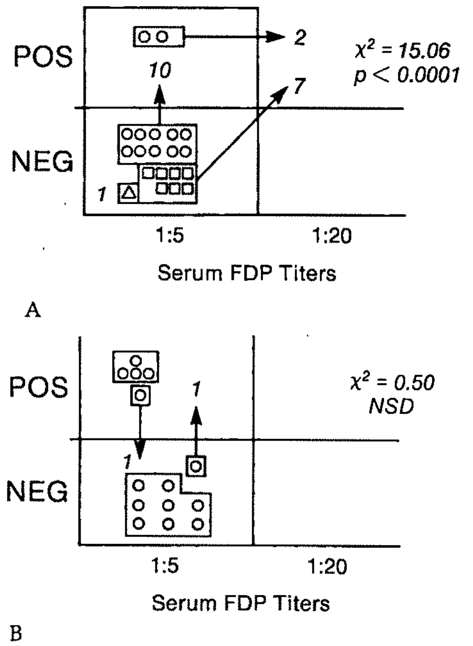

Fig 1. (A) Effect on serum fibrin degradation product (FDP) *titers of infusion of unwashed shed mediastinal blood* (SMB). *Each symbol represents 1 study patient. The symbols are located in the quadrant that represents the serum FDP titer of the patient before infusion of the unwashed SMB. Arrows are drawn from blocks of patients whose serum titer of FDP changed after the infusion. The number of patients and the change in titer are indicated by the quadrant in which the point of the arrow is located. Note that the FDP titer of only 1 patient remained unchanged after infusion of unwashed SMB. (B) Effect on serum FDP titers of infusion of washed SMB. The symbols are the same as in (A). After infusion, only 2 patients changed FDP titer. One patient with a previously negative* (NEG) *assay for FDP had a positive* (POS) *result, and 1 with a previously positive assay had a negative result.* (NSD = *no significant difference.)*

patients. Blundell [8] has been credited with the first literature report, in which he described autotransfusion in 10 women who had severe hemodynamic decompensation following postpartum hemorrhage. Except for sporadic reports in the literature, this treatment was overlooked until Klebanoff and Watkins [9] revised the technique for trauma victims during the Vietnam War. Citrate anticoagulant was added to a cardiotomy reservoir for collection of blood, which was reinfused rapidly with a roller pump.

Because there were dramatic successes and very few side effects, the Bentley Corporation (Bentley Laboratories, Inc, Irvine, CA) marketed this device with some modifications as the first commercially available autotransfuser. The Bentley device was withdrawn from the market after several deaths occurred due to infusion of massive amounts of air from the pressurized cardiotomy chamber [6]. Several devices with modifications of this basic principle are still in use at a variety of institutions for trauma and vascular surgery [10, 11].

Building on the successes of these devices, Symbas [12] began experiments and clinical studies on the autotransfusion of shed pleural blood obtained during chest trauma, his reasoning being that this blood was a readily available source of warm, compatible blood. He initially collected the blood in chest bottles with citrate anticoagulant, but after early experiments confirmed the blood was defibrinated and unclottable, he collected the blood in bottles with normal saline solution. However, a recent report by his group [13] stated that in rapid clinical bleeding, citrate is still added in the event the blood is not fully defibrinated.

The gynecological specialty provides clinical cases of rapid hemorrhage from ruptured ectopic pregnancies. Carty and co-workers [14] analyzed peritoneal shed blood and found it to be depleted of fibrinogen and factors V, VIII, and X. Also, it was low in platelets and had high titers of FDP. As ruptured ectopic pregnancies can lead to disseminated intravascular coagulation (DIC) and high FDP levels, they conjectured that autotransfusion of peritoneal blood obtained during operation could precipitate this problem, and recommended washing the shed blood to avoid the possibility of DIC and platelet dysfunction.

Reinfusion of SMB for cardiac surgical patients was a logical extension of the literature base built from experiences in trauma, vascular, and gynecological surgery. Schaff and colleagues [3] analyzed the constituents of SMB and found that this blood contained almost normal levels of factors VIII and IX, moderate platelet counts, and elevated levels of free hemoglobin and FDP. Comparing these findings with those in banked blood, they discovered the latter was acidotic, contained low levels of factors VIII and IX, and had minimal platelets and somewhat elevated levels of free hemoglobin. Schaff and co-workers concluded that the SMB was at least as good as banked blood. Clinical studies of SMB demonstrated no apparent hematological side effects and no difference in clinical bleeding between the groups receiving SMB or banked blood.

Table 5. Record of Blood Product Utilization

Product	Group 1 (Unwashed SMB) (n = 21)	Group 2 (Washed SMB) (n = 17)	Overall (n = 38)
Red blood cells			
Total units	8	17	
Patients tranfused	5 (24%)	7 (41%)	
Units/patient transfused	1.6	2.4	
Units/total patients	0.4	1.0	0.7
Fresh frozen plasma			
Total units	8	12	
Patients transfused	4 (19%)	4 (24%)	
Units/patient transfused	2.0	3.0	
Units/total patients	0.2	0.7	0.5
Platelets			
Total units	0	18	
Patients transfused	0	3 (18%)	
Units/patient transfused	0	6.0	
Units/total patients	0	1.1	0.5

SMB = shed mediastinal blood.

Table 6. Comparison of Postoperative Blood Loss and Homologous Transfusion Requirements for Adult Cardiac Surgical Patients

Reference	Year	Institution	No. of Patients	Mean Blood Loss[a] (mL/patient)	Homologous Blood[a] (mL/patient)
Morgan et al [25]	1972	Peter Bent Brigham Hospital	50	1,055 ± 90	3,500 ± 220
Kaplan et al [26]	1977	Emory University Hospital	60	825 ± 84	2,346 ± 232
Moran et al [27]	1978	Loyola University (Chicago)	25	1,118 ± 271	2,175 ± 175
Schaff et al [1]	1979	Johns Hopkins Hospital	271	912 ± 150	1,290 ± 91
Thurer et al [24]	1979	Cleveland Clinic	59	1,258	707
Johnson et al [23]	1983	Massachusetts General Hospital	168	1,160 ± 89	447 ± 60
Griffith et al [present report]	1989	University of California, San Diego	38	1,174 ± 98	300 ± 270

[a] Data are shown as the mean ± the standard error of the mean.

Bell [15] thought that SMB was of benefit over banked blood because of the presence of factors VIII and IX along with moderate numbers of platelets. However, recent work by Symbas's group [13] involving shed pleural blood showed marked decreases in the levels of factors VIII and V, moderate reductions in factors VII, X, XI, and XII, almost total absence of platelets and fibrinogen, and high levels of FDP. Only the factor IX level was near normal. These findings are remarkably similar to the findings of Carty and co-workers [14] in peritoneal blood. In addition, several authors [16, 17] reported that platelets obtained from autotransfusate do not aggregate normally to the usual stimuli of adenosine diphosphate, epinephrine, or collagen. Furthermore, radioactive serotonin studies and measurements of β-thromboglobulin levels showed that platelet release had taken place. This may result in platelet dysfunction [17, 18]. Together these data indicate that there are few platelets remaining in SMB and that they do not have normal function.

This study was prompted by a major difference between our experience with infusion of SMB and the data reported by Schaff and associates [3]. We found that infusion of unwashed SMB in cardiac surgical patients was routinely associated with the development of a positive test for FDP, thus raising the possibility of DIC. Consequently, one of the chief reasons we performed this study was to investigate the effect of the infusion of SMB on hemostasis; specifically, to ascertain whether the infusion of unwashed SMB was associated with DIC. Taken together, our clinical and laboratory data do not suggest the occurrence of DIC in these patients. This conclusion is supported by several lines of evidence, including the lack of a significant decrease in postinfusion fibrinogen or platelets, failure of the PT or PTT to become prolonged, and the negative protamine paracoagulation phenomenon in this group. In addition, the unwashed SMB group did not have increased bleeding after infusion. On the other hand, in nearly all patients who received unwashed SMB, tests became positive for FDP. Thus, our studies strongly suggest that the positive FDP assays in these patients were not due to DIC, but were a direct result of the infusion of high titers of FDP in the unwashed SMB. This is supported by our calculations of expected FDP titers, based on the known levels of FDP in the infusates (see Tables 2, 4). Washing the SMB both reduced the high levels of FDP (and free hemoglobin) and prevented the conversion of serum FDP assays after autotransfusion.

The induction of high levels of FDP in patients who receive unwashed SMB may be clinically significant. First, elevated levels of FDP may be additive to the effects of CPB in producing platelet dysfunction and may increase the likelihood of a bleeding diathesis. Levels of FDP greater than 25 μg/mL have been associated with serious clinical bleeding [19], possibly because of inhibition of platelet adhesiveness to connective tissue. These clinical findings are accompanied by laboratory evidence of decreased platelet aggregation in the presence of FDP by thrombin, adenosine diphosphate, and collagen stimuli [20, 21]. In this study, serum levels of FDP after transfusion of unwashed SMB were as high as 75 μg/mL (see Table 4), which is well above the level at which platelet dysfunction has been reported. Second, FDP may impair fibrin polymerization [22].

We were unable to demonstrate a clinical problem of increased bleeding from these theoretical disadvantages of infusing high titers of FDP. However, differences in blood loss or the use of blood products could easily be obscured by the significantly longer CPB time of the group receiving washed shed mediastinal blood, the fact that shed blood was not indexed to body weight, and the relatively small sample numbers. Although the differences in CPB time and the trend toward higher red cell use in this group may be in part due to a change in the surgical team, which included only the addition of a more inexperienced cardiothoracic surgical resident at the time studies in this group were undertaken, all other aspects of the study including operative technique, sample collection, and SMB washing were performed by one of us (L.D.G.) to decrease variability between groups.

Differences in clinical bleeding are difficult to demonstrate in any study because of patient variability. Table 6 adds our data regarding blood loss and replacement to a previously published table by Schaff and co-workers [1] and the experience of Johnson and associates [23] and Thurer and colleagues [24]. The mean blood loss in our patients was 1,200 mL per 24 hours, which compares favorably with that of the other groups. The amount of homologous blood transfused postoperatively has steadily decreased over the years from 3,500 mL per patient to our unusually low value of 300 mL per patient in this small number of study patients (our value includes all blood components). Part of the reason for this decrease is an awareness of the hazards of blood transfusion and the acceptance of lower postoperative hematocrits. In the past, some institutions [3] routinely maintained hematocrits at 35% in the postoperative period; now, the majority accept 30%. We allow the hematocrit to reach 22% without transfusion in patients without infarction, neurological problems, or congestive heart failure.

The success or failure of postoperative blood salvage should be judged largely on its influence on the use of homologous blood. Blood use in our patients, as a group, was very low (due in part to the routine use of intraoperative blood salvage), consequently making it more difficult to demonstrate differences in blood use. In this study, the mean equivalent of a blood unit we infused from SMB (and thus the amount of homologous transfusion avoided) was approximately 140 mL of packed red cells, which is the equivalent of slightly more than 0.5 unit of blood. The maximum amount of homologous blood saved in any patient was approximately 1.5 units (3 patients). In reviewing our administration of other blood products, platelet usage was found to be appropriate in the 3 patients to whom platelets were administered. It is also possible that the fresh frozen plasma could have been eliminated as recommended by Collins [28], as PTs are prolonged in the majority of patients after bypass and are not easily remedied by infusion of this product. The observed shortening of the PT after infusion in the group receiving unwashed SMB is not readily explainable in this study and does not fit with previously published results [6]. Further observations will be needed to determine if this is a reproducible difference.

In summary, this study compares some hematological effects of infusing washed or unwashed SMB into patients in the early postoperative period after CPB. The infusate was analyzed for hematocrit, FDP titers, and free hemoglobin. No significant differences were noted between groups in levels of fibrinogen, platelet counts, PT, PTT, or hematocrit at 24 hours except for an unexplained significant decrease in the postinfusion PT in the group receiving unwashed infusate.

This study, which involved relatively small numbers of patients, did not document an increase in either DIC or clinical bleeding in patients receiving unwashed SMB. It was clear, however, that infusion of this product produced elevated serum levels of FDP. The high titers of FDP in the unwashed SMB consistently converted the serum test for FDP to positive, whereas washing the SMB significantly decreased the FDP titers and prevented the conversion of the serum FDP test to positive. In a bleeding patient, the conversion of serum tests for FDP from negative to positive from infusion of unwashed SMB can confuse subsequent laboratory tests for DIC and might delay appropriate therapy or lead to empirical blood component transfusions.

This abnormality and a review of the literature suggest that potential but yet unproven hazards from the autotransfusion of unwashed SMB may outweigh the benefits. Until more specific tests are routinely available to rule out DIC, we recommend that strong consideration be given to washing SMB.

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Noninvasive Detection of Cardiac Allograft Rejection by Analysis of the Unipolar Peak-to-Peak Amplitude of Intramyocardial Electrograms

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The use of standard electrocardiographic monitoring to detect cardiac allograft rejection has become unreliable since the advent of cyclosporine immunosuppression. Unipolar peak-to-peak amplitude analysis has been shown to be a quantitative measure of ischemic myocardial injury. This study was performed to determine if unipolar peak-to-peak amplitude analysis could accurately detect cardiac allograft rejection as determined by blinded endomyocardial biopsies. Ten adult mongrel dogs underwent heterotopic (n = 7) or orthotopic (n = 3) cardiac transplantation with placement of sutureless screw-in electrodes (Medtronic, Inc, Minneapolis, MN) on the anterior and posterior aspect of each ventricle. Postoperatively, animals were immunosuppressed for seven to ten days with cyclosporine and prednisone and then allowed to reject the transplant. Digitally processed intramyocardial electrograms were obtained daily. Endomyocardial biopsy was performed 1 week postoperatively and then at three to five day intervals for histological correlation. A unipolar peak-to-peak amplitude decline of 15% or greater occurred one to three days before the biopsy detection in 10 of 10 episodes of rejection. There were no false negatives and one false positive (although a small focal lymphocytic infiltrate was present). Thus, noninvasive unipolar peak-to-peak amplitude analysis was 100% sensitive and 90% specific in predicting and detecting cardiac allograft rejection.

(Ann Thorac Surg 1989;47:407–11)

Before the advent of cyclosporine immunosuppression in 1980, standard electrocardiography was useful for detection of acute cardiac allograft rejection. Under azathioprine-based immunosuppressive protocols, a decreased voltage observed on the electrocardiogram (ECG) correlated with myocardial edema and lymphocyte infiltration [1, 2]. However, when immunosuppressive regimens are based on cyclosporine, episodes of acute allograft rejection are not accompanied by consistent ECG changes [3]. Analysis of the peak-to-peak amplitude of unipolar electrograms (R-wave voltage) obtained from intramyocardial plunge electrodes has been shown to be an accurate, sensitive, and quantitative predictor of local irreversible myocardial ischemic injury [4]. The unipolar peak-to-peak amplitude (UPPA) decrease correlates closely with the local histological changes that subsequently develop.

At present, the diagnosis of acute cardiac allograft rejection is most accurately made by serial percutaneous transvenous endomyocardial biopsies. Current protocols require at least 12 biopsies to be performed during the first 6 months after heart transplantation. Endomyocardial biopsy is invasive and expensive. Biopsies can only be performed in specialized centers, and necessitate a delay of 12 to 24 hours before results are available.

Unipolar peak-to-peak amplitude analysis provides the opportunity to monitor electrical changes in the myocardium continously. This study, in which orthotopic and heterotopic canine allografts were examined during the course of rejection, was performed to assess the ability of UPPA analysis to detect cardiac transplant rejection noninvasively.

Material and Methods

Experimental Thoracic Heterotopic Transplantation

Seven adult mongrel dogs received thoracic heterotopic cardiac transplants [5]. The heart from an unmatched donor dog was procured after preservation with potassium crystalloid cardioplegic solution and topical hypothermia with iced saline. An atrial septal defect was created by opening the fossa ovalis and the superior and inferior vena cavae were oversewn. Pulmonary veins were individually ligated. The donor aorta and pulmonary artery were prepared for anastomosis.

The recipient animal was anesthetized with sodium pentothal (1 mg/kg) and placed on a ventilator. Anesthesia was maintained with enflurane and succinylcholine. Through a left thoracotomy, the recipient superior vena cava and left innominate artery were mobilized. Anastomosis of the donor pulmonary artery to the recipient superior vena cava was performed with a continuous

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monofilament suture. Similarly, the donor aorta was anastomosed to the recipient left innominate artery. Upon restoration of blood flow and defibrillation, blood flowed through the allograft coronary arteries. The allograft did not contribute to the support of the systemic circulation (Fig 1).

Orthotopic Transplantation

Three animals underwent orthotopic cardiac transplantation as described by Lower and Shumway [6]. Mongrel dogs were anesthetized with sodium pentothol (1 mg/kg) and maintained under anesthesia with enflurane and succinylcholine. Donor hearts obtained from unmatched mongrel dogs were excised after arrest with potassium crystalloid cardioplegic solution and topical hypothermia with iced saline.

The donor heart was sutured in place following the conventional sequence of anastomoses. Hemodynamic and electrocardiographic monitoring were maintained until animals were stable, awake, and extubated.

All animals received humane care in compliance with the principles of laboratory animal care formulated by the National Society for Medical Research and the "Guide for the Care and Use of Laboratory Animals" prepared by the National Academy of Sciences and published by the National Institutes of Health (NIH Publication No. 80-23, revised 1978).

Electrodes

Sutureless intramyocardial screw-in electrodes (Medtronic, Inc, Minneapolis, MN) were placed on the anterior and posterior aspects of each ventricle at the time of operation. A standard indifferent electrode (Ethicon TPW-30 [Ethicon, Inc, Somerville, NJ] or Medtronic 6400 temporary myocardial pacing lead) was placed in the chest wall. All electrodes were brought out through a separate skin incision.

Immunosuppression Protocol

All recipient animals were given cyclosporine (10 mg/kg) and methylprednisolone (250 mg IV bolus) perioperatively. Postoperatively, administration of cyclosporine (10 to 20 mg/kg/day) and prednisone (1 mg/kg/day) was continued for seven to ten days to suppress rejection. Thereafter, immunosuppressive therapy was discontinued and the animals were allowed to reject their allografts.

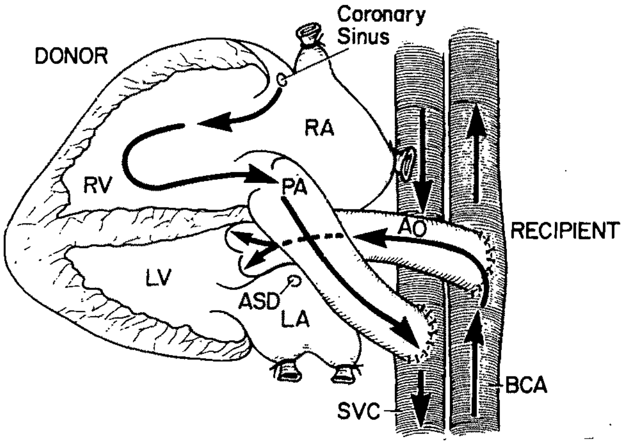

Fig 1. Experimental model of nonworking heterotopic cardiac transplant. (AO = aorta; ASD = atrial septal defect; BCA = brachiocephalic artery; LA = left atrium; LV = left ventricle; PA = pulmonary artery; RA = right atrium; RV = right ventricle; SVC = superior vena cava.)

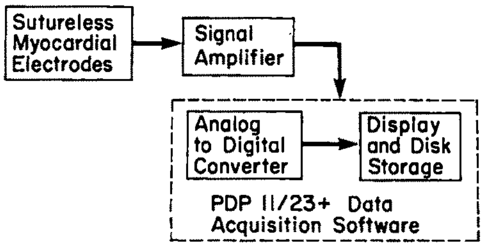
Sutureless Myocardial Electrodes
Signal Amplifier
Analog to Digital Converter
Display and Disk Storage
PDP 11/23+ Data Acquisition Software

Fig 2. Initial data acquisition system utilizing PDP 11/23+ computer and software designed in our laboratory.

Unipolar Peak-to-Peak Amplitude Data Acquisition

Intramyocardial electrograms were obtained daily. Data from all electrodes were obtained with simultaneous standard ECG. The initial data acquisition system we used is represented in Fig 2. Unipolar data from all four electrodes were amplified and filtered with a variable-gain signal amplifier. Filter settings were 1000 Hz high pass and 0.05 Hz low pass. Analog data were then digitized. Using a PDP 11/23+ computer and software designed in our laboratory, data were stored on 8-inch floppy discs and then analyzed using a separate analysis program (Fig 3). Later in the course of the study, a portable personal computer was coupled to a four-channel variable-gain signal amplifier and analog-to-digital converter. Using a commercially available software package (Asyst, MacMillan, Rochester, NY), data could be analyzed automatically (Fig 4).

Unipolar Peak-to-Peak Amplitude Analysis

Amplitudes for each channel were obtained by averaging 8 to 10 beats. During the first five days after implantation, the interaction between the screw electrodes and myocardium was inconsistent. Therefore, data analysis was begun on day 6. Daily UPPA values from each electrode were compared with the maximum voltage obtained in the three previous determinations (reference UPPA for that electrode). This ratio was expressed as a percentage. The change in UPPA expressed in percent was then averaged for all four electrodes. This value was defined as

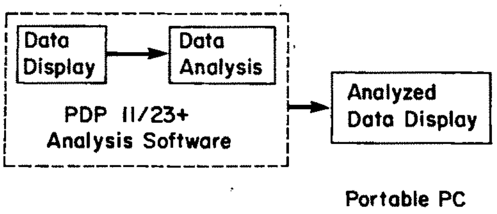

Fig 3. Initial data analysis system utilizing PDP 11/23+ computer and analysis software designed in our laboratory. Final calculations and graphics were facilitated by the use of a portable personal computer.

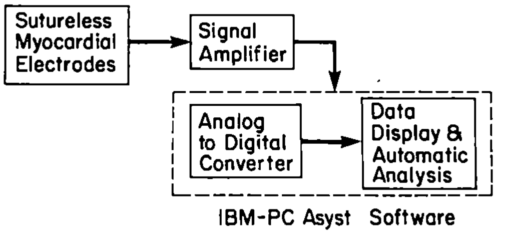
Sutureless Myocardial Electrodes
Signal Amplifier
Analog to Digital Converter
Data Display & Automatic Analysis
IBM-PC Asyst Software

Fig 4. Automatic data acquisition and analysis system based on a portable personal computer using a commercially available software package.

total percent reference UPPA. A total UPPA decline of greater than 15% (ie, less than 85% reference UPPA) was considered indicative of rejection.

Endomyocardial Biopsy

Endomyocardial biopsy specimens were obtained once during the initial period of immunosuppression and then every 3 to 5 days after cessation of cyclosporine and prednisone until animals were killed or died. At necropsy, full thickness sections of the left and right ventricle were submitted. Biopsy was performed using a standard cardiac biopsy forceps (Cordis Corp, Miami, FL). Dogs were lightly anesthetized with sodium pentothol and the right external jugular vein was exposed. Multiple specimens were obtained transvenously.

Histological Grading

All biopsy specimens and tissue obtained at postmortem examination were evaluated by a cardiac pathologist who was unaware of the UPPA findings or physiological state of the heart. Cardiac samples were graded histologically according to the criteria of Sibley and colleagues [7].

Control Group

Six normal animals had intramyocardial screw electrodes implanted in a fashion identical to that used in our experimental animals. These dogs were followed with daily UPPA analysis and standard ECG. Control group animals were followed 2 to 8 weeks.

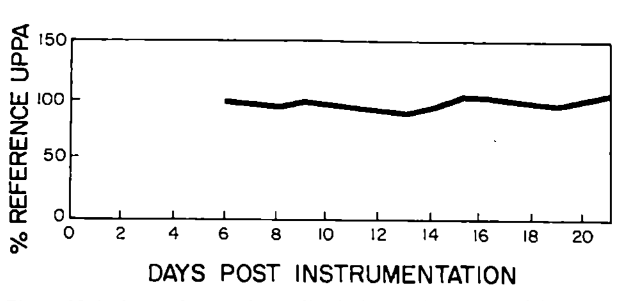

Fig 5. Unipolar peak-to-peak amplitude (UPPA) analysis of data obtained from a typical control animal. Total UPPA, expressed as a percentage of reference value, is plotted against time after instrumentation.

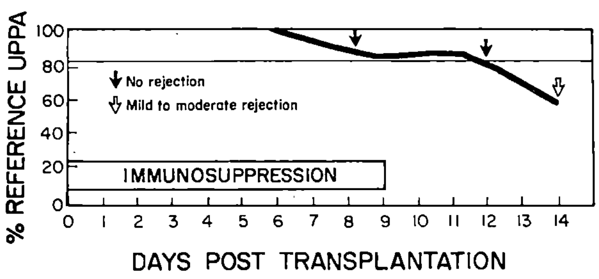

Fig 6. Unipolar peak-to-peak amplitude (UPPA) analysis of data obtained from a heterotopic allograft. Period of immunosuppression is indicated. Total UPPA, expressed as a percentage of reference value, is plotted against time after transplantation.

Results

Analyzed data for a typical control animal are shown in Figure 5. The total UPPA expressed as a percentage of its highest value from the previous three days (reference UPPA) is plotted against the days after instrumentation. A stable voltage pattern is observed over the 21-day course of monitoring. In all 6 animals there is no significant change in UPPA value, as these animals retain nearly 100% of the total reference UPPA value.

Figure 6 depicts the time course of UPPA changes seen in a heterotopically transplanted heart in which immunosuppressive therapy was maintained for nine days. The total UPPA, again expressed as a percentage of the reference value from the previous three days, is plotted against days after transplantation. In the first two biopsy specimens obtained, there was no rejection seen histologically. In the postmortem examination, mild to moderate rejection was seen. The UPPA value fell below 85% of reference on the 12th day after transplantation, a day in which endomyocardial biopsy revealed no evidence of rejection. This instance and three other instances in which endomyocardial biopsy was coincidentally performed on the first day of UPPA decline below 85% seem to indicate that a decline in UPPA may precede histological identification of rejection by one to three days.

Biopsy results are correlated with UPPA data in Table 1. In 10 biopsy specimens obtained during the initial period of immunosuppression in which no rejection was seen histologically, the UPPA values did not decline by more than 15%. There was one episode in which rejection was predicted by UPPA analysis, but histological examination revealed only a mild focal infiltrate and the specimen was consequently graded as having no rejection. This instance accounts for the only false positive result.

Table 1. Unipolar Peak-to-Peak Amplitude Data Compared With Histology

Average UPPA Decline	Rejection	No Rejection
<15%	0	10
>15%	10	1[a]

[a] Occurred in a heterotopic allograft.

UPPA = unipolar peak-to-peak amplitude.

In all 10 biopsy-documented episodes of rejection, there was a perfect correlation between UPPA analysis and histological findings. There were, therefore, no episodes of rejection that escaped detection by UPPA analysis. In total, there was a perfect correlation between UPPA analysis and histology in 20 of 21 biopsy specimens. By UPPA analysis, rejection was detected with 100% sensitivity and 90% specificity.

Comment

This study demonstrates that analysis of the UPPA of intramyocardial electrograms obtained from four electrodes is a highly sensitive and specific modality for detecting rejection in cardiac allografts. All episodes of graft rejection in both orthotopic and heterotopic allografts were predicted by an average UPPA decline of greater than 15%. In addition, it appears that a decrease in the UPPA value may actually precede rejection by one to three days.

Cellular changes in acute allograft rejection consist of edema, leukocytic infiltrate, and myocardial cell necrosis. These changes are responsible for alterations in the cardiac action potential in the involved area. Although it had previously been accepted that voltage decline in the standard ECG accompanied acute allograft rejection, the addition of cyclosporine to immunosuppressive regimens has altered this phenomenon. Electrocardiogram voltage can also be influenced by other conditions. The presence of pericardial or pleural effusion, severe edema, sepsis, pneumothorax, or pulmonary consolidation may all lead to decreased amplitude. Analysis of intramyocardial electrograms would have the advantage of assessing the whole heart while being independent of the variables that limit standard ECG analysis. This confirms previous observations that UPPA is unaffected by the functional status of the heart.

After being described by Sakakibara and Konno in 1962 [8], percutaneous transvenous endomyocardial biopsy was used as a method of monitoring heart transplant recipients in 1973 by Caves and his colleagues at Stanford [9]. Biopsy is performed at weekly intervals for 4 to 6 weeks and then at increasing intervals. During the first 6 months, at least 12 biopsies are performed.

Although histological evaluation of biopsy specimens remains the standard for evaluating graft rejection, it suffers from several limitations. Endomyocardial biopsy is an expensive technique that must be performed in a specialized center. Results may take 12 to 24 hours to be available, and in up to 6% of biopsies, inadequate tissue is obtained for proper assessment [10]. This invasive procedure also carries a small but real risk of complications. Pneumothorax and rupture of the right ventricle with hemorrhage have been reported.

Although the need for transvenous cardiac biopsy may not be eliminated, it would be desirable to limit the number of biopsies needed. Substitution of a noninvasive, reliable, cost-effective method of detecting rejection would seem to be the logical solution. Unipolar peak-to-peak amplitude analysis of intramyocardial electrograms fulfills these criteria, and the ability to telemeter the obtained data using standard available technology would make it completely noninvasive. Data acquisition and analysis could be computerized, thereby eliminating the need for highly trained personnel and expensive laboratory equipment.

Warnecke and associates [11] have recently correlated the decline of telemetered intramyocardial electrogram voltage from a single electrode with cardiac allograft rejection. Using a voltage decline of greater than 15%, they reported an 87.9% sensitivity for detecting rejection in human allografts. We believe that our 100% sensitivity is probably a result of using four electrodes. As the rejection process is occasionally patchy, four electrodes might detect an episode that would have been missed by a single electrode.

Avitall and co-workers [12] examined electrophysiological changes observed in a group of dogs receiving heterotopic transplants without immunosuppression. In their study, the authors found no correlation between changes in peak-to-peak amplitude and either mild or moderate rejection. There are several differences between the present study and theirs. In their model, ventricular electrograms were obtained from a single bipolar ring electrode on the surface of the right ventricle. Such an electrode would have the disadvantage of only sampling the sum of electrical activity directly beneath that electrode. Voltage changes should be detected with greater sensitivity by a unipolar intramyocardial electrode, which has the advantage of a larger, more transmural sampling area. In addition, no form of immunosuppression was used in the study of Avitall and co-workers. It would seem impossible to differentiate the effects of rejection from the short-term electrode-tissue interactions that Warnecke's group and our group found to prevent analysis of data during the initial five days after implantation. Finally, the present study's method of data analysis, in which daily UPPA values are compared with the data recorded over the preceding three days, tends to neutralize the more long-term effects of electrode-tissue interactions seen over weeks or months.

It is important to note that ischemia may also produce abrupt and substantial declines in the UPPA. This may become especially important in allografts developing atherosclerotic coronary artery disease. Exercise-induced regional ischemia could readily be identified by the local intramyocardial electrode in the ischemic region. This application of the UPPA would be useful in differentiating ischemia from chronic graft failure due to rejection as the cause of myocardial dysfunction in the long-term transplant recipient.

With the application of this technology, intervals between biopsies could be prolonged. If the average UPPA remains unchanged, biopsy could be safely postponed until it was indicated clinically. If a decrease in average UPPA greater than 15% was noted and rejection was clinically suspected, biopsy could be obtained for confirmation. As UPPA decline occurs early in the time course of acute allograft rejection, this information may lead to earlier detection of episodes of rejection, allowing treatment to be instituted more expeditiously, thereby limiting damage to the graft.

In conclusion, UPPA analysis using four intramyocardial screw-in electrodes provides a noninvasive, highly sensitive, and specific indicator of cardiac allograft rejection. Development of a four-channel computerized telemetry system may allow for an increased interval between biopsies and lead to earlier treatment of episodes of acute cardiac allograft rejection.

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Bronchial Carcinoids: A Review of 60 Patients

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Sixty patients with a bronchial carcinoid underwent surgical treatment. Preoperative fiberoptic bronchoscopy revealed a characteristic pink, smooth, bleeding tumor in 71.4% of the patients with a typical carcinoid and 16.7% of those with an atypical carcinoid ($p < 0.05$). Eight pneumonectomies, seven bilobectomies, 34 lobectomies, three lobectomies with bronchoplasty, six bronchotomies with bronchoplasty, and two segmental resections were performed. All patients entered follow-up, and 47 were followed for more than 5 years. Ten-year survival was 89.6% for patients with a typical carcinoid and 60% for those with an atypical carcinoid. Ten-year survival was 88.1% for patients with carcinoids without lymph node involvement. All patients with lymph node involvement died within 5 years. Overall, 5 of the 8 patients having pneumonectomy died of acute cardiorespiratory failure. We conclude that a limited surgical resection with or without bronchoplasty and systematic lymphadenectomy is the procedure of choice in patients with typical carcinoids. On the other hand, atypical carcinoids are comparable to well-differentiated malignancies of the lung. Whenever possible, pneumonectomy should be avoided in favor of bronchial sleeve resection.

(Ann Thorac Surg 1989;47:412–4)

Until recent decades, bronchial adenomas were considered to be slow-growing tumors with a negligible malignancy rate. However, several studies [1–3] have indicated that some of these neoplasms have a higher malignant potential, thus necessitating a review of their classification, prognostic criteria, and methods of treatment. Like small cell carcinoma of the lung, bronchial carcinoids are currently considered to arise from cells derived from the neuroectoderm, the so-called Kulchitsky cells [4].

The aim of the present study was to review our experience with a series of consecutive patients referred to our institution over a long period and having an adequate postoperative follow-up. The diagnostic criteria were assessed and the long-term results of surgical treatment evaluated by correlating histological features to patterns of recurrence and survival.

Material and Methods

From January 1968 to December 1987, 114 patients with bronchial adenoma underwent operation at the First Surgical Department of the University of Padua. The study population consisted of 60 consecutive patients who had a proven bronchial carcinoid and were operated on before December 1981. There were 35 male and 25 female patients, ranging in age from 13 to 66 years (mean age, 39 years).

All patients entered follow-up, and 47 survivors were followed for more than 5 years. The median follow-up was 114 months (range, 17 to 336 months). The surgical procedures were as follows: pneumonectomy, 8 patients; bilobectomy, 7; lobectomy, 34; lobectomy with bronchoplasty, 3; bronchotomy with bronchoplasty, 6; and segmental resection, 2. There were no operative deaths and no major postoperative complications. None of our patients received preoperative or postoperative radiation therapy or chemotherapy.

Classification of the carcinoid based on histological findings revealed 42 typical carcinoids and 18 atypical carcinoids. In 5 patients (8.3%), intraoperative frozen sections revealed metastatic involvement of mediastinal lymph nodes; all 5 patients had atypical carcinoids.

Two patients had reoperation for local recurrences. The first patient had undergone a left upper lobectomy for a "bronchial adenoma" in another hospital in 1956. He was seen with a recurrence in the left main bronchus in June 1974. Pneumonectomy was performed, and pathological examination showed an atypical carcinoid with lymph node metastases. The patient died of multiple bone metastases 7 years after reoperation. The second patient had undergone a lower bilobectomy for a typical carcinoid in February 1972. Almost 15 years later, in December 1986, an enlarged carinal lymph node was removed and found to have a metastasis of a typical carcinoid.

Survival curves were calculated according to the Kaplan-Meier method [5].

Results

The following symptoms were seen: recurrent or persistent pneumonia in 26 patients, hemoptysis in 11, cough in 5, and dyspnea in 5. Thirteen patients were asymptomatic, and the disease was detected on a chest roentgenogram.

The duration of symptoms was less than 1 year in 21

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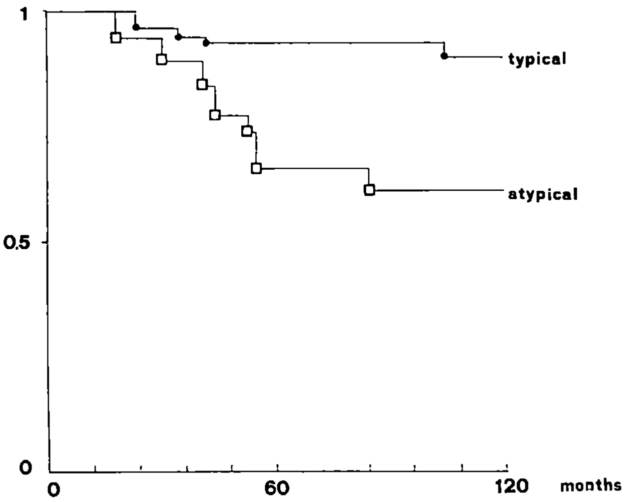

Fig 1. Survival curves for patients with typical and atypical carcinoids. The 10-year survival was 89.6% for those with typical carcinoids and 60% for those with atypical carcinoids.

patients, between 1 and 5 years in 15 patients, and longer than 5 years in 11 patients. Carcinoid syndrome developed in 3 patients (5%), early in the course of the disease in 2 and 10 years later in 1. Liver metastases of atypical carcinoid were diagnosed in these 3 patients.

All patients underwent preoperative fiberoptic bronchoscopy. In 50 patients, a bronchial obstruction was demonstrated: a somewhat characteristic pink, smooth, bleeding tumor that was not infiltrating in 33 patients; a pale tumor in 5; an extrinsic compression in 7; a neoplastic infiltration in 2; and an unspecified bronchial obstruction in 3.

Bronchoscopic results were negative in 10 patients. An endoscopic biopsy specimen of the bronchial lesion was obtained from 27 patients, and was positive in 18 (bronchial adenoma in 16, squamous cell carcinoma in 1, and anaplastic carcinoma in 1). In the remaining 9 patients, the biopsy result was negative.

Of the 42 patients with a typical carcinoid, 38 (90%) are alive at a minimum of 60 months to a maximum of 230 months postoperatively. Four patients have died: 1 in a road accident 43 months after operation, 1 of gastric cancer 24 months postoperatively, and 2 of acute pulmonary edema secondary to heart failure 36 and 108 months after operation. The 2 patients who died of myocardial failure had undergone pneumonectomy. The survival curve of this group of patients indicates a 5-year survival of 93% and a 10-year survival of 89.6% (Fig 1). Fifteen patients are alive and free of disease more than 10 years after operation.

Of the 18 patients with atypical carcinoids, 9 (50%) are alive at a minimum of 6 years to a maximum of 15 years after operation. Nine patients have died: 5 of multiple metastases at 300, 140, 53, 52, and 29 months after operation; 3 of acute cardiorespiratory failure 85, 40, and 17 months after pneumonectomy; and 1 of massive pulmonary embolism secondary to thrombophlebitis 43 months after operation. The survival curve indicates a 5-year survival of 66% and a 10-year survival of 60% (see Fig 1).

Comment

Reporting in 1954 a personal series of 41 bronchial adenomas in patients operated on at the Brompton Hospital, Price-Thomas [6] concluded that "the incidence of malignancy is so low that it is possible for practical purposes to ignore it."

However, some studies [1, 2, 7] have questioned the generic term *bronchial adenoma*; they underscore not only the different biological behavior of the three tumor types (ie, carcinoid, cylindroma, and mucoepidermoid), but also their varying degrees of malignancy. Because of these controversies, the ideal therapeutic strategy for patients with bronchial adenoma is still being debated.

We have attempted to define factors affecting survival in patients with bronchial carcinoids based on the long-term follow-up of a fairly large number of consecutive patients. Criteria of pathological diagnosis and principles of surgical treatment were homogeneous in our series, thus making worthwhile a critical evaluation of the results.

An accurate preoperative diagnosis is important to plan the appropriate treatment in patients with bronchial carcinoids. Clinical symptoms are unreliable, but should alert the physician to search for occult bronchial lesions. Carcinoid syndrome is always secondary to an atypical carcinoid and associated with liver metastases. The syndrome can appear late in the course of the disease, as in a patient in our series in whom symptoms developed after 10 years.

We believe that bronchoscopy plays a major role in the diagnosis of carcinoids. In our experience, an unequivocal aspect—pink, smooth, bleeding lobulation—is common, and was found in 30 (71.4%) of 42 patients with typical carcinoids and only 3 (16.7%) of 18 patients with atypical carcinoids ($p < 0.05$). Bronchoscopic biopsy significantly increases the diagnostic yield without adding morbidity. No bleeding was observed in our series. Consequently, in contrast to McCaughan and co-workers [8], we believe that biopsy of endobronchial lesions through a fiberoptic endoscope is a safe procedure and should be performed whenever the macroscopic aspect of the carcinoid is not diagnostic.

Typical carcinoids can, in general, be considered benign tumors. None of our 42 patients with such carcinoids had lymph node metastases. Long-term survival is high (93% at 5 years and 89.6% at 10 years), and no deaths in our series were related to regional or distant tumor spread. Recurrent disease occurred after 14 years in only 1 patient at the level of a carinal lymph node, and histological study demonstrated a typical carcinoid.

In our opinion, even though recurrences are an unusual finding in these patients, lymphadenectomy should be routinely performed to allow staging of the disease and, possibly, to prevent regional lymph node recurrences. In our series, the 2 deaths due to cardiac failure occurred in patients who had undergone pneumonectomy. Pneumonectomy should be avoided in patients with typical carcinoids and preference given to sleeve resection [9].

Atypical carcinoids, on the other hand, have a certain malignant potential. Five (27.8%) of our 18 patients had lymph node metastases, 1 had resection for bronchial recurrence, and 5 died of multiple metastases. Long-term survival was 66% at 5 years and 60% at 10 years. The same criteria used for lung cancer should therefore apply to this subtype of adenoma: macroscopically radical resection and adequate bronchial margins with hilar and mediastinal lymphadenectomy. Again, there were 3 deaths from heart failure in patients who had undergone pneumonectomy. This confirms that pneumonectomy should be avoided whenever feasible in favor of bronchial sleeve resection.

The negative prognosis related to lymph node metastases reported by other authors [1, 2] was confirmed in our series: we had no 5-year survivors among patients with lymph node metastases. Patients with lymphatic involvement died at 52, 43, 40, 29, and 17 months postoperatively. This is in contrast to the reports of McCaughan [8], Todd [10], and their associates, who noted a favorable prognosis even in the presence of lymph node metastases. We believe that the difference in these results could be due to the percentage of atypical carcinoids in each series.

The results of our long-term follow-up of patients treated for bronchial carcinoids indicate that typical carcinoids behave differently from atypical carcinoids. Although the former can be considered nearly benign tumors, the latter are comparable to well-differentiated malignancies of the lung. The difficulty of an accurate preoperative histological diagnosis constitutes a major drawback in treating patients with typical carcinoids. However, when the preoperative endoscopic aspect and frozen sections confirm this diagnosis and no lymph node metastases are found, a limited surgical resection, associated with bronchoplasty if necessary, is the procedure of choice.

Statistical analysis of the data was performed by Dr G. L. Pappagallo from the Department of Medical Oncology, ULSS 21, Padua, Italy.

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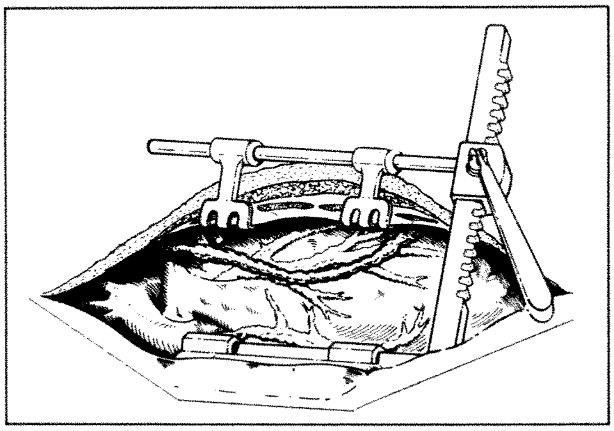

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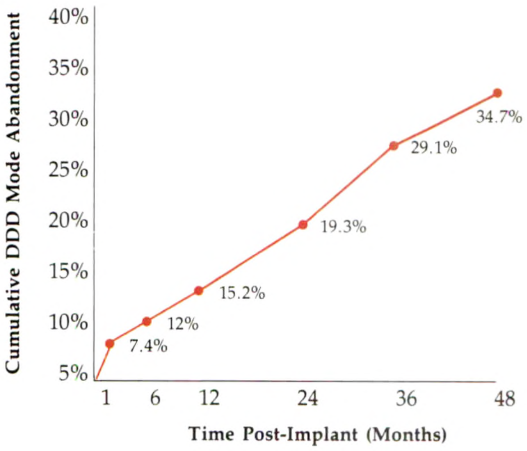

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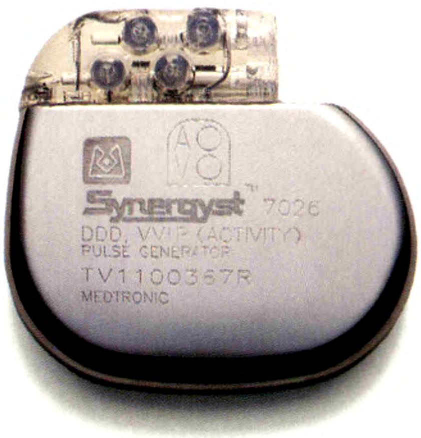

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[1] Atrial arrhythmias, loss of atrial sensing, sinus node dysfunction, atrial lead complications, chronotropic incompetence.
[2] Klementowicz, *PACE*, 10(2):409, Mar-Apr 1987.

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Bidirectional Cavopulmonary Shunts: Clinical Applications as Staged or Definitive Palliation

Ennio Mazzera, MD, Antonio Corno, MD, Sergio Picardo, MD, Roberto Di Donato, MD, Bruno Marino, MD, Dina Costa, MD, and Carlo Marcelletti, MD

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A standard Glenn anastomosis between the superior vena cava and the right pulmonary artery has been the accepted mode of treatment for patients with complex cyanotic congenital heart disease. We report our experience in 18 patients with such disease who underwent a bidirectional cavopulmonary shunt because of increasing cyanosis and growth cessation. All patients were considered less than "ideal" candidates for a Fontan procedure. We divided the patients into two groups: group 1 had azygos continuation and group 2 did not. Fourteen patients required hypothermic cardiopulmonary bypass. Bidirectional pulmonary blood flow was achieved in all patients. Only 1 death occurred (group 2). The improvement in oxygen saturation and overall clinical condition of these patients, together with the low mortality and morbidity, is encouraging. However, long-term follow-up is mandatory for a comprehensive evaluation of this surgical approach as definitive palliation or as a first stage for a Fontan operation.

(Ann Thorac Surg 1989;47:415–20)

The management of patients with complex cyanotic congenital heart disease (CCCHD) who are less than "ideal" candidates for a Fontan procedure because of the increasing risk of death is still a problem. However, a surgical approach is indicated in those patients with increasing cyanosis and growth cessation to increase effective pulmonary blood flow. One of the surgical options available is the cavopulmonary shunt. In 1951, Carlon and colleagues [1] demonstrated experimentally the feasibility of draining the systemic venous blood from the superior vena cava to the right pulmonary artery. Seven years later, Glenn [2] reported his experience using the standard cavopulmonary shunt to relieve cyanosis in patients with CCCHD. In 1966, Haller and co-workers [3] performed experimentally a cavopulmonary shunt without proximal ligation of the right pulmonary artery, and in this way obtained a bidirectional cavopulmonary shunt (BCS). In 1984, Kawashima and associates [4] reported successful palliation in patients with CCCHD using the BCS. However, little information is available on the use of this procedure as first-stage or definitive palliation [5–7]. We report our experience with the BCS in 18 patients with CCCHD.

Material and Methods

From October 1985 to July 1987, 18 patients underwent a BCS. For all patients, the indications for operation were increasing cyanosis and growth cessation. At the time of operation, all patients were considered less than ideal candidates for a Fontan procedure because of age (11 patients were less than 3 years old), mild insufficiency of the common atrioventricular valve (3 patients), presence of congenital or iatrogenic abnormalities of the pulmonary arteries (3 patients), or failure of a Fontan procedure (1 patient). The mean age at operation was 4.3 ± 2.9 years and the mean weight was 14.2 ± 5.7 kg.

The patients were divided into two groups: group 1 with azygos continuation and group 2 without azygos continuation (Table 1).

Fourteen patients had undergone previous surgical procedures. They included a classic or modified Blalock-Taussig shunt or central shunt (13 patients, 3 of whom required a second systemic–pulmonary artery shunt because of recurrent cyanosis) and a modified Fontan procedure (1 patient).

All operations were performed through a median sternotomy. In 2 patients, the BCS was done without hypothermic cardiopulmonary bypass, and 2 patients required a temporary heparinized superior vena cava–right atrium shunt. Fourteen patients underwent conventional hypothermic cardiopulmonary bypass. In 8 of these patients, a short period of circulatory arrest was necessary for adequate visualization because of relatively excessive collateral pulmonary blood flow. In all patients in whom cardiopulmonary bypass was used, the superior vena cava was cannulated near its junction with the innominate vein.

After division of the superior vena cava and transverse incision of the right pulmonary artery, continuous monofilament running sutures for the posterior anastomosis and interrupted sutures for the anterior anastomosis were used in all patients. Figure 1 illustrates a completed bidirectional cavopulmonary shunt. For patients in group 2, the azygos or the hemiazygos vein was ligated; in 6 of these patients, the proximal main pulmonary artery was ligated at the end of the procedure because of anterograde transvalvular pulmonary blood flow demonstrated by a

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Table 1. Summary of Patient Data

Patient No.	Age	Weight (kg)	Cardiac Anomalies	Previous Operation	Operation	Complication	Outcome
Group 1: Patients With Azygos Continuation							
1	2 yr 2 mo	10	Left isomerism, ventricular inversion, pulmonary atresia, single AV valve, DORV, TGA	Modified right Blalock-Taussig shunt	BCS	Pleuropericardial effusion	Alive and well
2	2 yr 11 mo	11	Left isomerism, PS, DORV, AVSD, persistent LSVC, hypoplastic left ventricle	None	BCS (small persistent LSVC occlusion)	None	Alive and well
3	6 yr 3 mo	19	Left isomerism, UVH, PS, AVSD, persistent LSVC, AV valve insufficiency	Modified left Blalock-Taussig shunt	Bilateral BCS, MPA occlusion	None	Alive and well
4	9 yr 4 mo	23	Left isomerism, PS, DORV, persistent LSVC, hypoplastic left ventricle, left PA distortion	Modified left Blalock-Taussig shunt	Bilateral BCS, MPA occlusion	None	Alive and well
Group 2: Patients Without Azygos Continuation							
5	4 yr	14	Dextrocardia, UVH, TGA, PS, right AV valve atresia, persistent LSVC, AV valve insufficiency	Modified left Blalock-Taussig shunt	Bilateral BCS, MPA occlusion	Pericardial effusion, right chylothorax	Alive and well
6	1 yr 3 mo	10	Dextrocardia, crisscrossed ventricle, VSD, PDA, persistent LSVC, TGA, PS	None	Bilateral BCS, PDA section	None	Alive and well
7	6 yr 2 mo	24	DORV, AVSD, PS, unroofed coronary sinus, persistent LSVC draining into left atrium, AV valve insufficiency	Classic left Blalock-Taussig shunt	Bilateral BCS, MPA occlusion	None	Alive and well
8	1 yr 5 mo	13	Left isomerism, PS, DORV, upside-down ventricles	None	BCS, MPA occlusion	None	Alive and well
9	9 yr 8 mo	21	UVH, PS, left PA hypoplasia	Modified left Blalock-Taussig shunt, central shunt	BCS, MPA occlusion	Pleuropericardial effusion	Alive and well
10	1 yr 3 mo	10	Pulmonary atresia, IVS, hypoplastic right ventricle, hypoplastic and stenotic left PA	Classic right Blalock-Taussig shunt, central shunt	BCS, plastic confluence PA, excision of tricuspid valve	None	Alive and well
11	2 yr 7 mo	11	cCTGA, pulmonary atresia, straddling AV valve, hypoplastic right ventricle	Classic right Blalock-Taussig shunt	BCS	None	Alive and well
12	2 yr 8 mo	11	cCGTA, pulmonary atresia, straddling AV valve, hypoplastic right ventricle	Classic right Blalock-Taussig shunt	BCS	None	Alive and well
13	5 yr 8 mo	25	UVH, left AV valve atresia, PS, TGA	Atrioseptectomy, modified Fontan	BCS, MPA occlusion	None	Alive and well
14	2 yr 10 mo	14	TA, PS	Classic right Blalock-Taussig shunt, central shunt	BCS	Pleural effusion, ascites	Alive and well
15	4 yr 9 mo	14	Pulmonary atresia + IVS, left coronary artery aneurysm, right PA stenosis	Classic right Blalock-Taussig shunt	BCS, excision of tricuspid valve	Pleural effusion	Alive and well

Table 1. Continued

Patient No.	Age	Weight (kg)	Cardiac Anomalies	Previous Operation	Operation	Complication	Outcome
16	1 yr 1 mo	10	Pulmonary atresia, cCTGA, VSD, straddling left AV valve	Modified right Blalock-Taussig shunt	BCS	Right chylothorax	
17	4 mo	6	Right isomerism, TAPVC, AVSD, common atrium, TGA, SP, AV valve insufficiency	None	BCS, MPA occlusion (3 mo after operation)	Right chylothorax	Late death
18	1 yr 10 mo	9	Left isomerism, situs inversus, DORV, AVSD, SP, persistent LSVC, common atrium	None	Bilateral BCS	None	Alive and well

AV = atrioventricular; AVSD = atrioventricular septal defect; BCS = bidirectional cavopulmonary shunt; cCTGA = congenitally corrected transposition of the great arteries; DORV = double-outlet right ventricle; IVS = intact ventricular septum; LSVC = left superior vena cava; MPA = main pulmonary artery; PA = pulmonary artery; PDA = patent ductus arteriosus; PS = pulmonary stenosis; TA = tricuspid atresia; TAPVC = total anomalous pulmonary venous connection; TGA = transposition of the great arteries; UVH = univentricular heart; VSD = ventricular septal defect.

pulsatile pressure curve in the superior vena cava. In 7 patients (3 in group 1 and 4 in group 2), the persistent left superior vena cava was anastomosed end-to-side to the left pulmonary artery during the same operation.

Associated surgical procedures were as follows: reconstruction of the pulmonary artery confluence in 2 patients, excision of the tricuspid valve in 2 patients with pulmonary atresia and intact ventricular septum, reconstruction of a surgically damaged innominate vein in 1 patient, and takedown of a Fontan procedure in 1 patient.

Results

The BCS was effective in relieving the cyanosis in all patients. Mean systemic oxygen saturation at room air increased in group 1 from 76.5% ± 3.8% before operation to 89% ± 5.2% ($p < 0.005$) in the control measurement immediately before hospital discharge, and in group 2, from 72.6% ± 6.6% to 87.8% ± 3.3% ($p < 0.005$) (Table 2).

Mean pressure in the superior vena cava measured early in the postoperative period was 8 ± 3 mm Hg in group 1 and 9 ± 2 mm Hg in group 2. In 6 patients (group 2), the main pulmonary artery was ligated to allow only mild to moderate elevation of systemic venous pressure in the superior vena cava because of substantial transvalvular pulmonary blood flow. In 12 patients the transvalvular pulmonary blood flow was judged not substantial, and the main pulmonary artery was left open. Cardiopulmo-

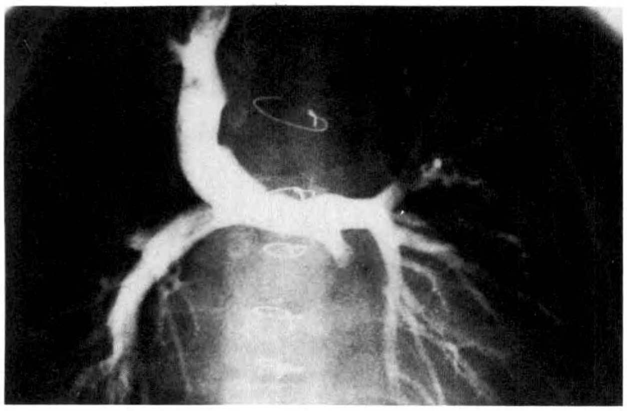

Fig 1. The right superior vena cava is anastomosed to the right pulmonary artery, thus creating a bidirectional cavopulmonary shunt.

Table 2. Systemic Oxygen Saturation[a]

Patient No.	Preoperative	Early Postoperative	Late Postoperative
Group 1			
1	72	87	85
2	75	83	83
3	78	91	88
4	81	95	89
Group 2			
5	78	83	85
6	83	86	86
7	79	90	86
8	80	89	86
9	75	80	80
10	63	88	84
11	65	91	87
12	69	90	86
13	67	92	83
14	78	87	88
15	81	91	89
16	73	88	93
17	65	88	. . .
18	70	86	84

[a] Data are shown as percentages.

nary bypass was necessary for 14 patients. For 4 patients this was because acute occlusion of the right pulmonary artery was not tolerated and for the remaining 10 patients, because we considered the risk of cardiopulmonary bypass low and the advantage high of performing the anastomosis under the best surgical conditions.

Seven patients had a persistent left superior vena cava. In these patients a variation of the BCS was performed, namely, a connection of the left superior vena cava to the left pulmonary artery. In this way, a bidirectional and bilateral cavopulmonary shunt was achieved with a more balanced pulmonary blood flow and a lower superior vena cava pressure.

No hepatic, renal, or myocardial failure occurred in the immediate postoperative period. The postoperative period was uneventful in 11 patients. Seven patients experienced complications: pleural effusion or pleuropericardial effusion in 5 and chylothorax in 2. Two of the 5 with pleuropericardial effusion required thoracentesis, 2 required pericardial drainage, and 1 required maximum diuretic therapy. In 2 patients with chylothorax, surgical ligature of the damaged thoracic duct was necessary.

Follow-up ranged from 6 to 26 months (mean follow-up, 16 months). In all patients the cardiothoracic ratio decreased, and normal growth was observed. The dose of digoxin or diuretics, or both, was reduced in 14 patients and eliminated in the remaining 4 patients. Mean systemic oxygen saturation on room air, measured at the last control by a pulse oximeter (model 3700, Biox Ohmeda), was 85% ± 2.3% in group 1 and 86% ± 2.7% in group 2. During exercise, systemic oxygen saturation decreased in group 1 to 81% ± 3% and in group 2, to 82% ± 3%.

Fifteen patients were restudied; 4 underwent cardiac catheterization (see Fig 1) with angiography and 11 underwent lung scintigraphy with a technetium 99m lung perfusion scan. Although bilateral pulmonary blood flow was present in all patients studied, superior vena cava blood flow through the BCS tended to be greater in the right lung. In particular, the mean value of lung perfusion in 11 patients without a persistent superior vena cava was 65% in the right lung and 35% in the left lung. In the 7 patients in whom a persistent left superior vena cava was anastomosed end-to-side to the left pulmonary artery, lung perfusion values were 57% and 43% in the right and left lung, respectively. The flow was not balanced in patients 5, 6, and 11 because of a hypoplastic pulmonary artery.

The youngest patient died 13 months after operation. Catheterization was performed 3 months postoperatively for recurrent cyanosis and demonstrated a mean superior vena cava pressure of 15 mm Hg and mild to severe atrioventricular insufficiency. For this reason we decided to ligate the main pulmonary artery. However, the mean superior vena cava pressure decreased only slightly, and the patient died of superior vena cava thrombosis.

Comment

The Fontan procedure has been extensively applied in cases of CCCHD with excellent results when patients were considered ideal candidates [8–10]. However, the patients in our study were considered less than ideal for the Fontan procedure because of age (11 were less than 3 years old), mild insufficiency of the common atrioventricular valve (3 patients), presence of congenital or iatrogenic abnormalities of the pulmonary arteries (3 patients), or an unsuccessful Fontan procedure (1 patient). Surgical results for such patients are characterized by increased mortality and morbidity [11, 12], and thus the management of patients for whom operation is indicated because of recurrent cyanosis and growth cessation remains a problem. The surgical options for these patients are: a conventional systemic–pulmonary artery shunt, a standard Glenn shunt, a BCS, or an unconventional surgical procedure such as that proposed by the Mayo Clinic group [13]. This last option is associated with high mortality.

The advantages of the standard Glenn shunt over the conventional systemic–pulmonary artery shunt are as follows: reduced work load for the systemic ventricle, decreased blood flow through the right atrium, venous blood shunt rather than an arteriovenous mixture, and the absence of late-developing pulmonary vascular obstructive disease in the right lung. In short, the standard Glenn shunt allows an increase of effective pulmonary blood flow without an increase in heart work load [14–16]. The BCS presents further advantages over the standard Glenn shunt: continuity between the right pulmonary artery and the left pulmonary artery is preserved, bilateral pulmonary blood flow is obtained, and the option for any subsequent procedure is still available.

In our experience, the BCS in patients with CCCHD who are not ideal candidates for a Fontan procedure increased effective pulmonary blood flow in both lungs and thus increased systemic oxygen saturation. This increase in systemic oxygen saturation can occur in patients with azygos continuation (group 1) because this approach is, with the exception of the hepatic and coronary venous return, a complete bypass of the right ventricle. In patients without azygos continuation (group 2), we can speculate that it is due to a diversion of more desaturated venous blood drained from the superior vena cava directly into the pulmonary arteries. Although the increase of systemic oxygen saturation after operation that we obtained may appear suboptimal if considered as an absolute value, the association of mild to moderate improvement in systemic oxygen saturation with reduction in cardiac work load substantially improved the clinical condition, as demonstrated by the decrease of the cardiothoracic ratio, normal growth, and the reduction of medication. Some doubt still remains as to the observed decrease in systemic oxygen saturation during exercise, which correlated inversely with a rise in cardiac output. It is possible that the significant increase in coronary sinus and inferior vena cava return following the rise in cardiac output during exercise leads to the increase in desaturated blood reaching the aorta.

There were fewer postoperative complications for patients with azygos continuation (group 1) after a BCS than were reported after the Fontan procedure. This could be explained by the different hemodynamic pattern observed in the patients with a BCS in whom the hepatic and renal venous returns drain into a low-pressure atrial chamber with a very low or zero incidence of hepatic or renal failure as shown by our data. Coronary sinus venous return also empties into a low-pressure atrial chamber, thereby reducing the risk of myocardial failure during the immediate postoperative period [17–19]. In addition, we found the mean pressure in the superior vena cava to be lower for 12 patients with a BCS in whom we considered the transvalvular pulmonary blood flow not substantial when compared with ideal patients after a Fontan procedure. This may explain the very low incidence (2 of 12 patients) of pleuropericardial effusion that we observed.

In addition, the BCS could be considered long-term palliation after failure of a Fontan procedure. In fact, the BCS could avoid the sudden reduction of ventricular compliance that can be one of the reasons for failure of the Fontan principle in patients with a previous ventricular work load.

One limitation in use of the BCS could be the presence of severe atrioventricular incompetence. In this case, we agree with Kawashima and co-workers [4] that the BCS should be performed with valve replacement. In the case of mild or moderate atrioventricular valve incompetence, we postulate that a reduction of the ventricular work load and diversion of the superior vena cava return directly into the pulmonary arteries could reduce the hemodynamic effect of the incompetence.

We observed 1 late death in our series. The youngest patient died of superior vena cava thrombosis. It is possible that we underestimated the insufficiency of the atrioventricular valve. These patients may need antiaggregant or anticoagulant drugs, as suggested by some authors [20–22] for patients with a Fontan procedure.

Long-term follow-up is mandatory before a final conclusion can be reached, particularly in regard to the incidence of arteriovenous fistula, venous collateral, or changes in caval blood flow direction, as observed after the standard Glenn shunt [23–25]. However, we speculate that the positive effects of an increase in systemic oxygen saturation, the presence of low pulmonary pressure, and the bilateral distribution of pulmonary blood flow could reduce the risk of these complications.

In conclusion, in patients considered less than ideal candidates for a Fontan procedure but in whom the Fontan criteria might be met in the future, the BCS should be considered as first-stage palliation. However, if for any reason the Fontan procedure is considered a high risk (as could be the case for patients 5, 6, and 11) or if the Fontan procedure fails, the BCS should be considered as long-term palliation.

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Notice From the Southern Thoracic Surgical Association

The Thirty-sixth Annual Meeting of the Southern Thoracic Surgical Association will be held at the Phoenician Golf and Tennis Resort, Scottsdale, AZ, November 9–11, 1989. There will be a $155 registration fee for nonmember physicians except for guest speakers, authors and coauthors on the program, and residents. There will be a $50 registration fee for attendees of the Postgraduate Course, which will be held the morning of Thursday, November 9, 1989. The Postgraduate Course will provide in-depth coverage of thoracic surgical topics selected primarily as a means to enhance and broaden the knowledge of practicing thoracic and cardiac surgeons.

Members wishing to participate in the Scientific Program should submit an original abstract and one copy by May 15, 1989, to Bradley M. Rodgers, MD, Program Chairman, Southern Thoracic Surgical Association, 111 East Wacker Drive, Chicago, IL 60601. Abstracts must be submitted on the Southern Thoracic Surgical Association abstract submission form. These forms may be obtained from the Association's office or in this issue of *The Annals of Thoracic Surgery*. All slides used during the presentation must be 35 mm. Manuscripts of accepted papers must be submitted to *The Annals of Thoracic Surgery* prior to the 1989 meeting or to the Secretary-Treasurer at the opening of the Scientific Session.

Applications for membership should be completed by July 1, 1989, and forwarded to Hooshang Bolooki, MD, Membership Committee Chairman, Southern Thoracic Surgical Association, 111 East Wacker Drive, Chicago, IL 60601.

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Internal Mammary Artery Grafts: The Shortest Route to the Coronary Arteries

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Inadequate length can limit the use of the internal mammary artery (IMA) for coronary revascularization. By following the shortest route from its origin to the recipient coronary artery, IMA use can be maximized. Seven cadavers were studied to determine that shortest route for the left and right IMAs. The shortest route for the left IMA to the left anterior descending coronary, diagonal, and circumflex coronary arteries was through the pericardium ($p \leq 0.01$). For the right IMA, the significantly shortest routes were across the anterior heart for the left anterior descending and diagonal arteries, through the right pericardium for the right coronary artery or posterior descending artery, and through the pericardium and transverse sinus for the circumflex artery. Thus, any coronary artery can be reached with an in situ IMA, and the route through the pericardium is markedly shorter to ipsilateral coronary arteries.

(Ann Thorac Surg 1989;47:421–7)

For coronary artery bypass grafting, the internal mammary artery (IMA) graft carries a greater long-term patency, a decreased need for reoperation, and, perhaps, a decreased recurrence of angina when compared with the saphenous vein graft [1–5]. However, the number and length of IMAs limit their use. Numerous methods of extending the use of IMA grafts have been suggested, including augmenting their length by multiply transecting the fascia in the IMA pedicle [6, 7], constructing sequential grafts [7–11], using free IMA grafts by constructing an aorta–IMA anastomosis [7, 11, 12], using both IMAs [7, 9, 13, 14], using both limbs of the IMA beyond its bifurcation [9], gaining length by dissecting the artery well down into the rectus muscle [7], and choosing the shortest route from the IMA origin to the recipient coronary artery [2, 7, 8, 10, 11, 15].

This study was designed to find the shortest route for each IMA to each feasible recipient coronary artery.

Material and Methods

Seven autopsies were performed through the usual Rokitansky incision on 3 men and 4 women. Measurements were made of the patient's weight, height, and sternal lengths, and, on each side, the length of the IMA from its origin to the fifth intercostal space and to the costal margin (Table 1; Fig 1).

The pericardium was opened in the midline. Then measurements were made from the origin of the IMA to each of the following feasible coronary arteries: right (RCA), posterior descending (PDA), cicumflex marginal, diagonal, and left anterior descending (LAD).

All measurements were made under the following conditions:

1. The cadaver was intubated with a cuffed endotracheal tube, usually through a tracheostomy.
2. An Ambu bag was used to inflate the lungs to an extent approximating full inspiration before each measurement.
3. Measurements were taken from a string draped without slack from the origin of the IMA to the coronary artery. Care was taken to avoid so much tension on the string that it would cut into tissues.
4. On a given coronary artery, the measurement was always made to the same point, that to which a coronary graft would most commonly be performed.

All statistical comparisons were performed using paired *t* tests (RS 1 statistical program) to assess differences between any two pertinent measurements on the same individual, thus obviating the need to normalize measurements between individuals. A *p* value of less than 0.05 was considered significant.

Table 1. Group Description

Variable	Value[a]
Age	59 ± 12.75
Weight (kg)	71.9 ± 25.4
Height (cm)	165.5 ± 11.4
S–G (cm)	16.4 ± 1.9
S–X (cm)	20.4 ± 1.9
LIMA–ICS (cm)	17.4 ± 1.1
LIMA–CM (cm)	22.1 ± 1.1
RIMA–ICS (cm)	17.5 ± 1.6
RIMA–CS (cm)	22.2 ± 0.6

[a] Data are shown as the mean ± the standard deviation.

CM = costal margin; ICS = fifth intercostal space; LIMA = origin of left internal mammary artery; RIMA = origin of right internal mammary artery; S–G = sternal notch to junction between xiphoid and sternum; S–X = sternal notch to xiphoid tip.

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Table 2. Distance From Internal Mammary Arteries to Coronary Arteries

Route	Distance[a] (cm)	Probability of Null Hypothesis			
		1	2	3	4
LIMA–LAD					
O	17.79 ± 2.00	0.002	0.002		
M	15.57 ± 1.27	0.01			
P	14.14 ± 1.03				
LIMA–Diag					
O	18.41 ± 2.24	0.001	0.001		
M	15.71 ± 1.47	0.003			
P	13.43 ± 1.05				
LIMA–Cir					
O	22.43 ± 3.35	0.001	0.001		
M	19.21 ± 3.86	0.01			
P	16.21 ± 2.36				
RIMA–LAD					
O	17.29 ± 2.41	0.23	0.006		0.002
P	18.49 ± 3.43	0.03		0.004	
PT	20.50 ± 2.61	0.001			
OT	21.86 ± 2.50				
RIMA–Diag					
O	16.07 ± 1.62	0.008	0.001		0.004
P	18.10 ± 2.61	0.41		0.22	
PT	18.71 ± 2.14	0.16			
OT	19.50 ± 2.94				
RIMA–RCA					
O	16.07 ± 0.89	0.10			
P	15.14 ± 1.89				
RIMA–PDA					
O	20.14 ± 2.25	0.014	0.049		0.003
P	18.00 ± 1.53	0.001		0.001	
PT	23.07 ± 3.51	0.027			
OT	24.50 ± 3.25				

[a] Data are shown as the mean ± the standard deviation.

Cir = circumflex marginal coronary artery; Diag = diagonal coronary artery; LAD = left anterior descending coronary artery; LIMA = left internal mammary artery; M = medial-to lung; O = over lung (LIMA) or pericardium (RIMA); OT = over pericardium, through transverse sinus; P = through pericardium; PDA = posterior descending coronary artery; PT = through pericardium, through transverse sinus; RCA = right coronary artery; RIMA = right internal mammary artery; 1 = between adjacent values; 2 = between first and third values; 3 = between second and fourth values; 4 = between first and fourth values

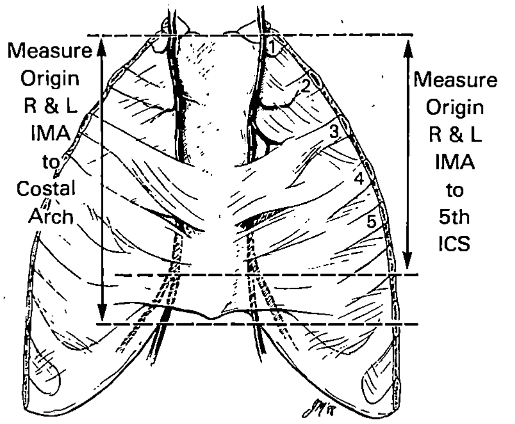

Fig 1. Posterior view of sternal plate with internal mammary artery (IMA) *measurements from origin to the fifth intercostal space* (5th ICS) *and to the costal arch.* (L = *left;* R = *right.)*

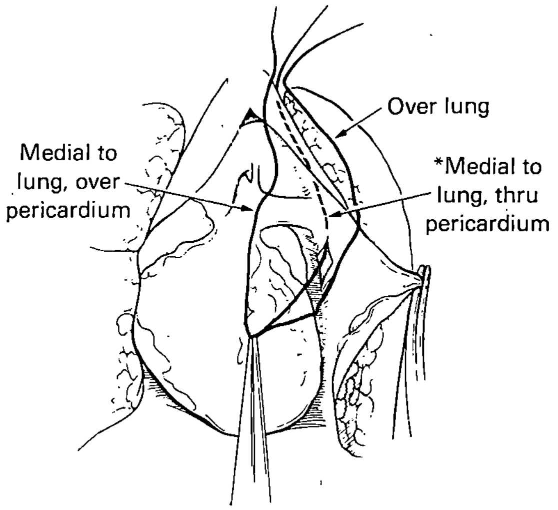

Fig 2. Measurements of three routes from origin of left internal mammary artery to left anterior descending coronary artery. (= shortest route.)*

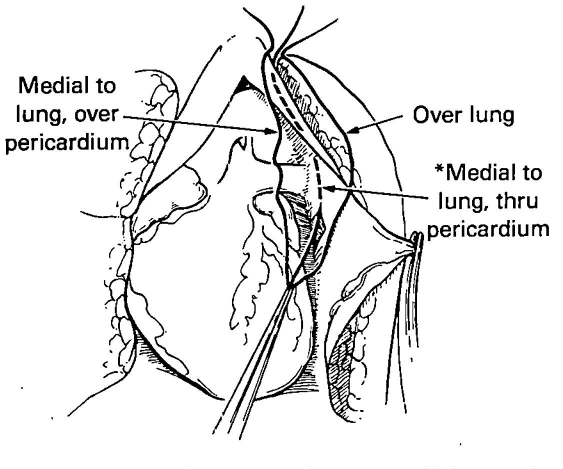

Fig 3. Measurements of three routes from origin of left internal mammary artery to diagonal artery. (= shortest route.)*

The following measurements were made from the IMA origin to the coronary artery (Tables 2, 3; Figs 2–9):

Left IMA (LIMA) to LAD, diagonal, and circumflex over anterior surface of left lung.

LIMA to LAD, diagonal, and circumflex medial to left lung.

LIMA to LAD, diagonal, and circumflex medial to left lung and through a pericardial incision immediately anterior to the left phrenic nerve.

Table 3. Distance From Right Internal Mammary Artery to Circumflex Artery

Route	Distance[a] (cm)	Probability of Null Hypothesis				
		OR	OL	PR	PL	PT
OR	24.64 ± 4.97	. . .	. . .	. . .	. . .	. . .
OL	21.07 ± 3.27	0.120	. . .	. . .	. . .	. . .
PR	23.79 ± 3.92	0.440	0.09	. . .	. . .	. . .
PL	19.75 ± 4.50	0.130	0.59	0.150	. . .	. . .
PT	18.79 ± 2.80	0.002	0.13	0.003	0.67	. . .
OT	20.71 ± 3.96	0.016	0.81	0.078	0.72	0.04

[a] Data are shown as the mean ± the standard deviation.

OL = over pericardium, over heart to left side; OR = over pericardium, around right side of heart; OT = over pericardium, through transverse sinus; PL = through pericardium, over heart to left side; PR = through pericardium, around right side of heart; PT = through pericardium, through transverse sinus.

Right IMA (RIMA) to LAD and diagonal over the right pericardium and anterior to the heart.

RIMA to LAD and diagonal through a pericardial incision immediately anterior to the right phrenic nerve and anterior to the heart.

RIMA to LAD and diagonal through a pericardial incision immediately anterior to the right phrenic nerve and through the transverse sinus.

RIMA to LAD and diagonal over the pericardium and through the transverse sinus.

RIMA to circumflex over the right pericardium and along and under the right side of the heart.

RIMA to circumflex over the right pericardium and over the aorta and pulmonary artery around the left side of the heart.

RIMA to circumflex through the pericardium and along and under the right side of the heart.

RIMA to circumflex through the pericardium and over the aorta and pulmonary artery around the left side of the heart.

RIMA to circumflex through the pericardium and through the transverse sinus.

RIMA to circumflex over the pericardium and through the transverse sinus.

RIMA to RCA over the pericardium.

RIMA to RCA through the pericardium.

RIMA to PDA over the pericardium.

RIMA to PDA through the pericardium.

RIMA to PDA through the pericardium and through the transverse sinus.

RIMA to PDA over the pericardium and through the transverse sinus.

To determine the feasibility of various grafts, the measurements just listed were subtracted from the measured IMA lengths. All calculations were performed only on individual cadavers, but only the mean of the differences is expressed (Tables 4, 5).

Results

The IMA lengths to the fifth intercostal spaces were 17.4 cm and 17.5 cm on the left and right sides, respectively. Measured to the costal margins, the lengths were 22.1 cm

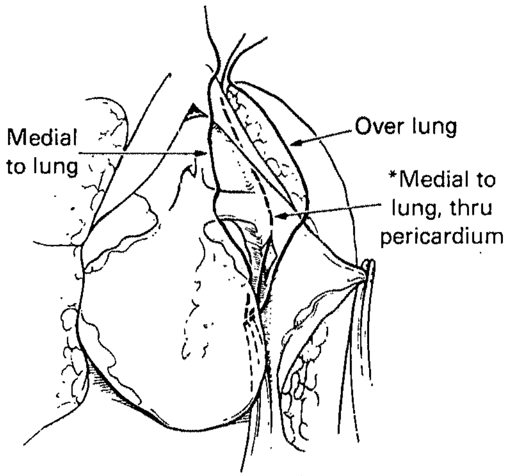

Fig 4. Measurements of three routes from origin of left internal mammary artery to circumflex artery. (= shortest route.)*

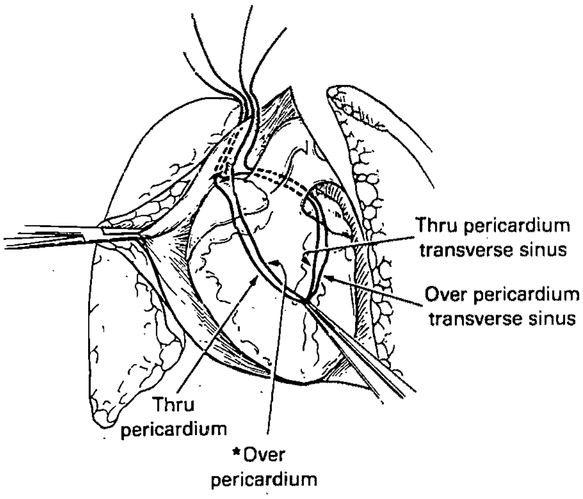
Thru pericardium transverse sinus
Over pericardium transverse sinus
Thru pericardium
*Over pericardium

Fig 5. Measurements of four routes from origin of right internal mammary artery to left anterior descending coronary artery. (= shortest route.)*

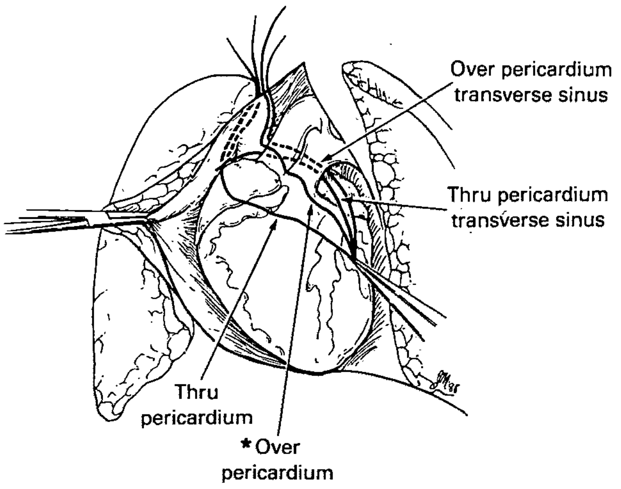

Fig 6. Measurements of four routes from origin of right internal mammary artery to diagonal artery. (= shortest route.)*

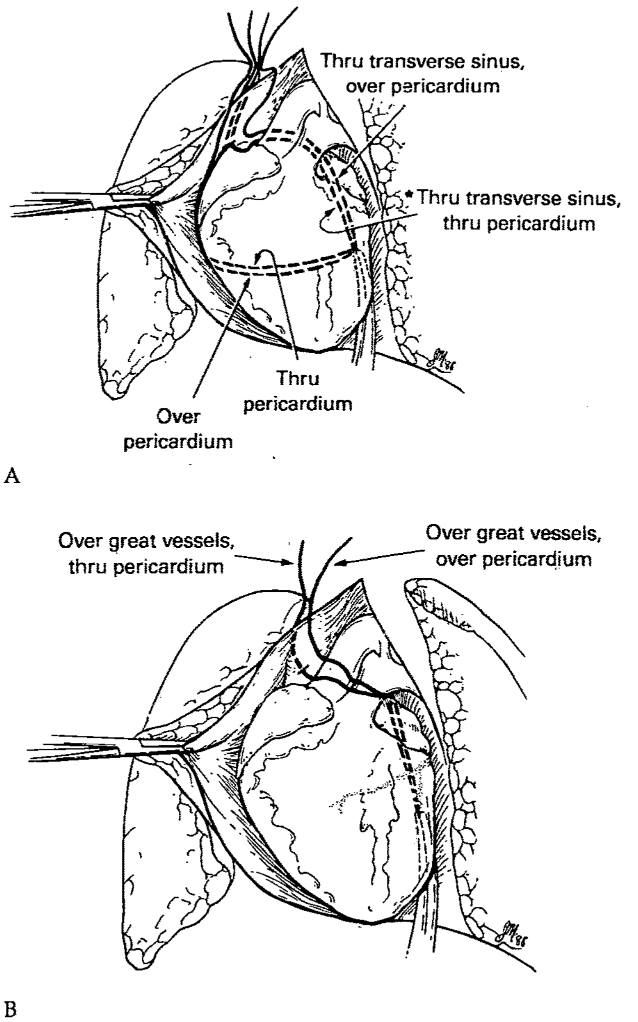

Fig 7. (A) Measurements of four routes from origin of right internal mammary artery to circumflex artery. (B) Measurements of two routes anterior to the aorta from origin of right internal mammary artery to circumflex artery. (= shortest route.)*

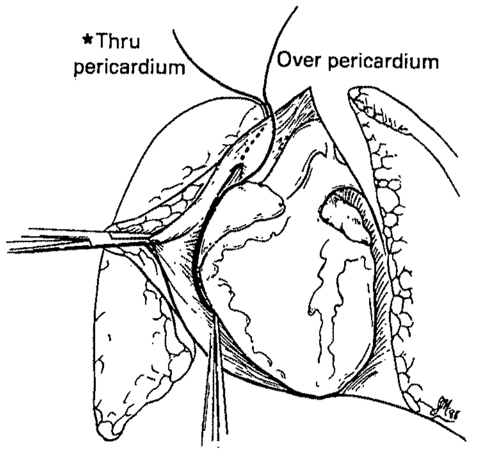

Fig 8. Measurements of two routes from origin of right internal mammary artery to right coronary artery. (= shortest route.)*

and 22.2 cm for the left and right, respectively (see Table 1).

The distances from the IMA origin to the coronary arteries, using the indicated different routes, are shown in Tables 2 and 3. For the LIMA to the LAD, the shortest route is through the pericardial incision; distances were 17.79 cm over the lung, 15.57 cm medial to the lung, and 14.14 cm through the pericardium. Each value differs significantly from each other ($p < 0.05$).

For the LIMA to the diagonal, the shortest route is also through the pericardial incision; distances were 18.41 cm over the lung, 15.71 cm medial to the lung, and 13.43 cm through the pericardial incision. Each of these values differs significantly from each other.

For the LIMA to the circumflex, the shortest route is again through the pericardial incision; distances were 22.43 cm over the lung, 19.21 cm medial to the lung, and 16.21 cm through the pericardial incision. Each of these values differs significantly from each other.

For the RIMA to the LAD, the shortest distance is the direct path over the pericardium to the artery; distances were 17.29 cm over the pericardium, 18.49 cm through the

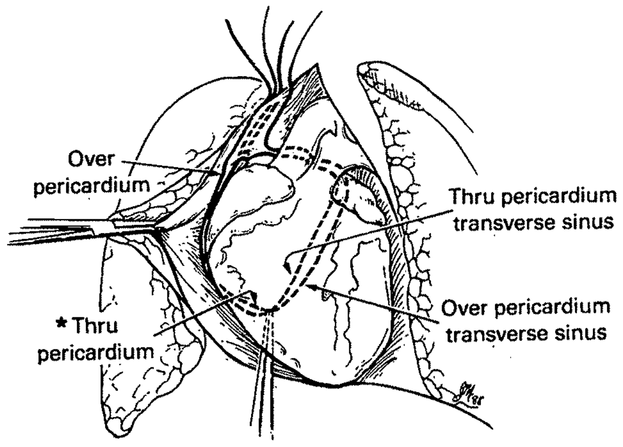

Fig 9. Measurements of four routes from origin of right internal mammary artery to posterior descending coronary artery. (= shortest route.)*

Table 4. Length of Left Internal Mammary Artery Minus Distance to Coronary Arteries[a]

Route	O	M	P
Left Anterior Descending			
LIMA–ICS	−0.43	1.79	3.21
LIMA–CM	4.29	6.50	7.93
Diagonal			
LIMA–ICS	−1.06	1.64	3.93
LIMA–CM	3.66	6.36	8.64
Circumflex			
LIMA–ICS	−5.07	−1.86	1.14
LIMA–CM	−0.36	2.86	5.86

[a] Data are shown as the mean value in centimeters.

CM = costal margin; ICS = fifth intercostal space; LIMA = left internal mammary artery; M = medial to lung; O = over lung; P = through pericardium, medial to lung.

right pericardial incision, 20.5 cm through the pericardium and the transverse sinus, and 21.86 cm over the pericardium and through the transverse sinus. The direct (anterior) path is significantly shorter than both routes through the transverse sinus but not significantly shorter than the anterior route through the pericardial incision.

For the RIMA to the diagonal, the shortest distance is again the direct (anterior) path over the pericardium to the artery; distances were 16.07 cm over the pericardium, 18.10 cm through the pericardium, 18.71 cm through the pericardium and transverse sinus, and 19.50 cm over the pericardium and through the transverse sinus. The direct (anterior) path is significantly shorter than all the other routes.

For the RIMA to the circumflex, the shortest distance is through the pericardium and transverse sinus. This route is significantly shorter than all other routes except the route anterior to the aorta and pulmonary artery and through the right pericardial incision ($p = 0.67$).

For the RIMA to the RCA, the slightly shorter distance is through the pericardial incision, 15.14 cm compared with 16.07 cm over the pericardium ($p = 0.10$).

For the RIMA to the PDA, the shortest route is through the pericardial incision and following the course of the native RCA; distances were 20.14 cm over the pericardium, 18.00 cm through the pericardium, 23.07 cm through the pericardium and transverse sinus, and 24.50 cm over the pericardium and through the transverse sinus. The shortest route is significantly so compared with all the other routes.

We also compared the IMA lengths with distances to arteries. The measured distances to the arteries, subtracted from the measured lengths of the IMAs, are shown in Tables 4 and 5.

When measured to the fifth intercostal space, the LIMA was always sufficiently long to reach the LAD or diagonal coronary artery provided that the shortest route (through the pericardium) was used. Even with this route, however, the LIMA was occasionally too short to reach the circumflex artery. Measured to the costal margin, the LIMA was always long enough to reach any of these three coronary arteries provided that the route through the pericardium was used.

Using the RIMA measured to the costal margin and using the shortest route (over the pericardium and heart), the RIMA was always sufficiently long to reach the LAD or diagonal coronary artery. When measured to the fifth intercostal space, the RIMA was often too short to reach

Table 5. Length of Right Internal Mammary Artery Minus Distance to Coronary Arteries[a]

Route	O	P	PT	OT	OR	OL	PR	PL
Left Anterior Descending								
RIMA–ICS	0.21	−0.99	−3.00	−4.36	. . .	. . .	. . .	. . .
RIMA–CM	4.93	3.73	1.71	0.36	. . .	. . .	. . .	. . .
Diagonal								
RIMA–ICS	1.43	−0.60	−1.21	−2.00	. . .	. . .	. . .	. . .
RIMA–CM	6.14	4.11	3.50	2.71	. . .	. . .	. . .	. . .
Circumflex								
RIMA–ICS	. . .	. . .	−1.29	−3.21	−7.14	3.57	−6.29	−2.88
RIMA–CM	. . .	. . .	3.43	1.50	−2.43	1.14	−1.57	2.50
Right								
RIMA–ICS	1.43	2.36	. . .	. . .	. . .	. . .	. . .	. . .
RIMA–CM	6.14	7.07	. . .	. . .	. . .	. . .	. . .	. . .
Posterior Descending								
RIMA–ICS	−2.64	−0.50	−5.57	−7.00	. . .	. . .	. . .	. . .
RIMA–CM	2.07	4.21	−0.86	−2.29	. . .	. . .	. . .	. . .

[a] Data are shown as the mean value in centimeters.

CM = costal margin; ICS = fifth intercostal space; O = over lung; OL = over pericardium and over heart to left side; OR = over pericardium and right side; OT = over pericardium, through transverse sinus; P = through pericardium; PL = through pericardium and over heart to left side; PR = through pericardium and around right side of heart; PT = through pericardium, through transverse sinus; RIMA = right internal mammary artery.

either the LAD or the diagonal. Using any other than the shortest path, the RIMA to the costal margin length was often too short to reach the LAD or diagonal in individual cases, although the means of the differences were positive, thus indicating an average excess length of RIMA.

For the circumflex artery, no combination of RIMA or route always gave a sufficient excess of RIMA length over distance to the coronary artery. However, the RIMA to the costal margin length routed through the pericardium and transverse sinus or routed through the pericardium and over the aorta and pulmonary artery was too short in only 1 patient each, and the mean of the differences was positive (RIMA more than long enough to reach) for both routes.

Using the RIMA measured to the costal margin, the RIMA was always sufficiently long to reach the RCA, but did so with more artery to spare when routed through the pericardial incision.

The only combination of RIMA that always reached the PDA was RIMA to the costal margin length routed through the pericardial incision.

Comment

Compared with the saphenous vein, the IMA has a greater patency and produces a decreased long-term mortality when used as a coronary artery graft [1–5]. In an effort to extend the use of the IMA, we evaluated the shortest course from IMA origin to the recipient coronary artery.

All coronary arteries could be reached with one or both in situ IMAs. However, with only two arteries, regardless of methods to find the best route to the coronary artery, it is unlikely that more than two coronary beds can be revascularized with IMAs. Also, Tector [9] made the point that not all of the heart can be revascularized with IMA grafts, and suggested that they be used primarily to graft the left-sided vessels, thus leaving the right coronary arteries to be grafted with saphenous vein. His rationale for this allocation of IMAs is that the RIMA to the RCA or PDA carries a higher occlusion rate than it does to the left system or than does the LIMA, in part (he speculates) because the right lung has a greater tendency to kink the RIMA than does the left lung to kink the LIMA.

In the performance of the measurements for this study, it was obvious that any IMA crossing anterior to the heart to the opposite side had little or no risk of interference from the ipsilateral lung. However, any IMA coursing along the ipsilateral side of the heart can be in jeopardy from the lung on the same side with the danger of stretching the graft or kinking the anastomosis. By routing these grafts posterior and medial to the apex of the lung and then through the pericardium, one obtains the shortest course and the course with the least jeopardy from the adjacent lung.

For revascularization of the left-sided coronary arteries with the LIMA, the route through the pericardium proves to be consistently and considerably shorter to the LAD, diagonal, and circumflex arteries than any other route. These results are confirmed by clinical studies by Pacifico [15], Jones [7], and their colleagues. For the LAD and diagonal, and usually for the circumflex, the IMA transected at the fifth intercostal space will be sufficiently long to reach those coronary arteries. Sequential grafts require more length and hence require a more distal dissection of the IMA. It has been our clinical experience that the LIMA is usually of sufficiently large caliber below its bifurcation to be usable.

To revascularize the LAD and diagonal with the RIMA, the shortest course, as would be expected, is the direct one over the heart. If transected at the level of the fifth intercostal space, the RIMA will often be too short; it should therefore be dissected down to and transected at the costal margin. As routing the RIMA across the anterior surface of the heart exposes it to considerable danger in coronary reoperations, the slightly longer course through a pericardial incision might be wiser, because it then allows for pericardial closure over the graft.

If the RIMA is transected at the costal margin, it will almost always be sufficiently long to reach the circumflex branch arteries. Although passing it through the pericardium and through the transverse sinus proves to be the shortest course, the route over the aorta and pulmonary artery may be as good for proximal branches.

For both the RCA and PDA, the shortest course for the RIMA is through the pericardium. To consistently reach the PDA, the RIMA must be divided near the costal arch.

In the performance of the measurements for this study, several caveats must be raised. First, the measurements can be somewhat subjective. The lungs must be inflated to the same extent for each measurement. The same degree of tension must be kept in the measuring string. These variables were minimized by having the same individual (T.J.V.) make all measurements. Second, the conditions in a cadaver cannot reproduce those in a living patient. Cardiac fullness, for example, differs between life and death, and so does cardiac compressibility. Also, the heart and lungs of the cadaver lie quiescent. Third, the conclusions drawn from these measurements presume that the IMAs will be usable at the measured levels of transection (at the fifth intercostal space or costal arch). Finally, the decreased patency of RIMA grafts to the right coronary arterial system and the increased technical difficulty of peforming these anastomoses may create clinical reluctance to proceed, even though this study demonstrates that the RIMA should be sufficiently long.

This study suggests other possible studies. The assessment of the coronary arteries accessible with free IMA grafts and the shortest route for them (or for saphenous vein grafts) could be made from a similar series of measurements originating at the aortic root. The feasible combinations of sequential IMA grafts could similarly be determined.

The conclusions reached from this study are as follows:

1. Any coronary artery can be reached with an in situ IMA graft.
2. The shortest course to ipsilateral coronary arteries is medial to the lung and through the pericardium.
3. No conceivable frugality of IMA routing can allow the revascularization of more than two coronary beds; saphenous vein or another conduit such as gastroepi-

ploic artery still must be employed to revascularize the third.

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Incidence of Residual Defects Determining the Clinical Outcome After Correction of Tetralogy of Fallot: Postoperative Late Follow-up

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The postoperative results in 150 patients who had repair of tetralogy of Fallot (mean follow-up, 10.2 ± 2.6 years) were defined as good in 71.3%, fair in 20.7%, and unsatisfactory in 8.0% on the basis of clinical criteria. Ninety-six percent of the patients are socially active, 92.0% have a good exercise tolerance, and 79.3% participate in sports. Data from 78 postoperative hemodynamic studies show mild right ventricular dysfunction in almost all patients examined. Peak systolic right ventricular/left ventricular pressure ratio decreased in the postoperative period in 65.4% of patients, remained unchanged in 3.8%, and increased in 30.8%. Minimal residual anomalies can modify the prognosis substantially. Of our patients, 53.3% of those with a shunt ($p < 0.05$), 37.5% of those with stenosis (not significant), and 53.8% of those with pulmonary incompetences (p = not significant) have fair or unsatisfactory results. The associated defects are particularly unfavorable. Rhythm and conduction disturbances have resulted in fair or unsatisfactory results in 65.1% of patients. Such a disturbance occurring soon after bypass must be considered an incremental risk factor: 52.9% of patients seen with rhythm and conduction disturbances show the same disturbances later ($p < 0.001$).

(Ann Thorac Surg 1989;47:428–35)

Tetralogy of Fallot is a well-known malformation clinically, morphologically, and surgically [1–8]. However, an organized multicenter investigation and the identification of homogeneous classes for the comparison of data present some objective difficulties because tetralogy of Fallot encompasses a wide spectrum of morphological subsets. These subsets range in several series from associated ventricular septal defect (VSD) with right ventricular outflow tract obstruction (RVOTO) to associated double-outlet right ventricle.

Nevertheless, the repair of tetralogy of Fallot gives good chances of excellent short-term and midterm results both hemodynamically and functionally [1, 3, 4, 9, 10]. In the long term, the results are more doubtful [1, 4, 11–14]. These doubts concern the following: tolerance of pulmonary regurgitation; tolerance of residual shunts and gradients; incidence of, type of, and prognosis for rhythm or conduction disturbances, or both; and possible application of a two-stage repair in select patients and age ranges.

To verify our results in patients with a follow-up longer than 11 years, we reviewed the initial series of 150 consecutive patients who underwent correction of tetralogy of Fallot at Centre Médico-Chirurgical de la Porte de Choisy, Paris, before 1975.

Material and Methods

From January 1969 to December 1975, 150 patients with tetralogy of Fallot (VSD + RVOTO due to anterosuperior displacement of the infundibular septum; mitral and aortic continuity; aortic overriding of 50% or more) underwent repair by the same surgical team at our institution. Mean age at operation was 9.2 ± 3.3 years (range, 2.5 to 26 years).

We divided this consecutive series of patients into three groups according to the anatomical pattern (Table 1). Group 1 comprised 16 patients (10.7%) with normal pulmonary ring, trunk, and branches and mild RVOTO at the ventricular and valvular levels. Group 2 had 75 patients (50.0%) with normal pulmonary ring, trunk, and branches and severe RVOTO at the ventricular and valvular levels. Group 3 comprised 59 patients (39.3%) with a hypoplastic pulmonary ring and trunk. In group 3, 22.0% of the patients (8.7% of all patients) were seen with stenosis either of the right or left branch or of the bifurcation.

All patients were operated on with cardiopulmonary bypass (CPB) and intermittent aortic cross-clamping (a rectal temperature of about 30°C was used before 1972 and about 22°C since 1972). The VSD was closed using a right ventricular (RV) approach with a patch sewn directly on the septal crista. Interrupted stitches were used on the lower border of the VSD and the "risk" area, and an uninterrupted suture was used on the remaining circumference. The RVOTO was relieved without placing any

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Table 1. Anatomical and Surgical Characteristics of and Preoperative Data on 150 Patients With Tetralogy of Fallot

Group	No. of Patients	Age (yr)			Hematocrit (%)		Associated Cardiac Anomalies	Associated Complications and Malformations	Palliation				Low Output Syndrome
		<5	5–10	>10	<50	>50			Total	Blalock	Blalock & Blalock	Blalock & Waterston	
1. Normal annulus; no patch	16 (10.7%)	0	12 (75.0%)	4 (25.0%)	10 (62.5%)	6 (37.5%)	Muscular VSD (1), anomalous CA (1), aberrant LSA (1)	Hemiplegia (1), scoliosis (1)	8 (50.0%)	8 (100%)	0	0	4 (25.5%)
							Total 18.8%	Total 12.5%					
2. Normal annulus; ventricular patch	75 (50.0%)	5 (6.7%)	47 (62.7%)	23 (30.7%)	34 (45.3%)	41 (54.7%)	Subaortic stenosis (1), TAPVD (1), LSVC (4), SI + LSVC (1), aberrant LSA (4), anomalous CA (4), anomalous CA + aberrant LSA (1)	Cerebral abscess (1), scoliosis (1), cerebral abscess + scoliosis (1), psychic handicap (3), endocarditis (1), esophageal atresia (1)	53 (70.7%)	50 (94.3%)	3 (5.7%)	0	17 (22.7%)
							Total 21.3%	Total 10.7%					
3. Hypoplasia of annulus, trunk, and/or branches; transannular patch[a]	59 (39.3%)	5 (8.5%)	37 (62.7%)	17 (28.8%)	24 (40.7%)	35 (59.3%)	AI (1), multiple VSDs (1), SI (1), TAPVD (1), LSVC (1), PI + pulmonary aneurysm (1), RPA thrombosis (1), anomalous CA (1), anomalous CA + VSD (1)	Endocarditis (1), hemiplegia + psychic handicap (1), myxedema (1), renal failure (1), subclavian artery aneurysm (1)	45 (76.3%)	38 (84.4%)	3 (6.7%)	4 (8.9%)	14 (23.7%)
							Total 15.3%	Total 8.5%					

[a] 46 patients (78.0% of group 3) had hypoplasia of the annulus and trunk; 13 (22.0%) had hypoplasia of the annulus, trunk, and branches.

AI = aortic incompetence; CA = coronary artery; LSA = left subclavian artery; LSVC = left superior vena cava; PI = pulmonary incompetence; RPA = right pulmonary artery; SI = situs inversus; TAPVD = total anomalous pulmonary venous drainage; VSD = ventricular septal defect.

Table 2. Criteria for Evaluating Postoperative Results After Repair of Tetralogy of Fallot

	Criterion					
Grade	NYHA Class	Performance[a]	Therapy	Cardiothoracic Ratio	Rhythm Anomaly	Complications
Good	I	Good	None	<0.55	None	None
Fair	I	Fair[b]	Medical	0.55–0.60	Anomaly not requiring therapy	Minor with complete relief
Unsatisfactory	II–IV	Handicap[b]	Reoperation	>0.60	Anomalies requiring medical or surgical therapy	Major

[a] Performance refers to social and school performance. [b] This was not considered if present preoperatively and if not necessarily related to the operation.

NYHA = New York Heart Association.

patch in group 1, with a ventricular patch in group 2, and with a transannular patch in group 3.

Infundibular stenosis that could not be relieved by a simple resection was treated with a triangular patch, the base of which was sutured to the pulmonary ring. Hypoplasia of the annulus and the trunk with a good bifurcation or with stenosis of the left branch was treated with a transannular patch extending to the left branch to guarantee good ramification of the right branch and to reduce the risk of residual stenosis of the trunk. Stenosis of the bifurcation was repaired with a double patch: one over the infundibulum, annulus, trunk, and left branch and the other over the right branch. Peripheral stenosis beyond the pericardial reflection did not occur. One patient with thrombosis of the left branch underwent right monopulmonary repair. In 1 patient, the right branch had to be reimplanted because of very severe stenosis at the origin. No coronary anomalies necessitating a prosthetic conduit were encountered. Clinical, anatomical, and surgical data are listed in Table 1.

Early and late postoperative results were graded good, fair, or unsatisfactory according to specific clinical criteria (Table 2). Also, the type of rhythm recovery after CPB and its relation to the previous rhythm and the rhythm at follow-up were analyzed.

The data from 78 catheterizations (55 of them performed consecutively on an elective basis 3 weeks postoperatively) and the RV to left ventricular (LV) pressure ratio in the early period after CPB and at the first and second catheterizations were analyzed (Tables 3, 4). We noted occupation, exercise tolerance, and sports activities when relevant.

Table 3. Hemodynamic Data at End of Cardiopulmonary Bypass

	RV Pressure (mm Hg)			RV/LV Pressure Ratio		
Group	<50	50–75	>75	<0.50	0.50–0.75	>0.75
1	10	6	0	10	6	0
2	67	5	3	61	12	2
3	53	6	0	45	13	1

LV = left ventricular; RV = right ventricular.

Results

Hospital mortality was 9.0%. Four patients (2.7%) were lost during follow-up. Mean follow-up for all 150 patients was 10.2 ± 2.6 years (range, 5 to 17 years).

The results after repair of tetralogy of Fallot in the three groups were graded good, fair, or unsatisfactory by the criteria shown in Table 2. In group 1, 87.5% had a good result, and 12.5% had a fair result; no result was unsatisfactory. In group 2, 69.3% had a good result, 18.7% had a fair result, and 12.0% had an unsatisfactory result. In group 3, 69.5% had a good result, 25.4% had a fair result, and 5.1% had an unsatisfactory result. In all, 71.3% of patients had a good result, 20.7% had a fair result, and 8.0% had an unsatisfactory result. There were no significant differences between the three groups ($\chi^2 = 5.37$; $p =$ not significant [NS]). The reasons for the determination of a fair or unsatisfactory result are shown in Table 5.

Of the 150 patients, 92.0% (138) showed a good exercise tolerance, and 79.3% (119) engaged in some form of sports. Social activity could be considered normal in 96.0% (144). Four patients were behind in school, and 2 had a psychic handicap not necessarily related to the operation. The postoperative complications included hemiplegia (1 patient), a pineal tumor (1), epilepsy (1), Blalock permeable (4), phrenic nerve paralysis (1), and chylothorax (1).

There is a residual permanent shunt (pulmonary/systemic flow ratio > 1) in 9.3% (14/150). The mean shunt is 10.7% ± 6.6% (range, 3% to 25%). In 71.4%, the shunt is at the ventricular level; in 21.4%, at the atrial level; and in 7.1%, at both the ventricular and atrial levels. Six (30.0%) of the 20 shunts disappeared.

A residual RVOTO (RV pressure > 50 mm Hg or RV/LV pressure ratio > 0.50 or pressure gradient [Δp] > 30 mm Hg) occurred in 16.0% of patients (24/150) with a mean Δp of 38.8 ± 11.3 mm Hg (range, 20 to 55 mm Hg). In 50.0% of patients, the Δp was at the bifurcation; in 41.7%, at the infundibular and valvular levels, and in 8.3%, at the valvular level. When at the bifurcation level, stenosis was prevalent on the right branch: in 41.7%, in isolation, and in 58.3%, in association with the left branch.

Pulmonary incompetence (PI) was clinically present in all patients in whom repair was accomplished with a transannular patch. On the basis of ventricular diastolic

Table 4. Hemodynamic Data at Postoperative Catheterization[a]

Group	Right Atrial Pressure (mm Hg)	RV Pressure (mm Hg)	Pressure gradient (mm Hg)	Left Atrial Pressure (mm Hg)	RV/LV Pressure Ratio
1	7.7	54.1	27.0	9.0	0.55
2	6.6	47.2	20.6	8.7	0.42
3	7.1	46.8	19.3	7.8	0.47
	5.7[b]	43.3[b]	20.7[b]	5.3[b]	0.42[b]

[a] Data are shown as the mean. [b] This is the value for the subgroup with stenosis of branches.

LV = left ventricular; RV = right ventricular.

loading, it was considered clinically significant on angiography or pulsed Doppler cross-sectional echocardiography in 8.7% of all patients (13/150).

A residual shunt and residual stenosis were present in 6.7% of patients (10/150); a residual shunt and major PI, in 3.3% (5/150); residual stenosis and major PI, in 2.7% (4/150); and a residual shunt, residual stenosis, and major PI, in 2.0% (3/150).

Of the 150 patients, 12.7% (19) did not have substantial dilation of the RV outflow tract. Major aneurysms (7 patients, 4.7%) were definitely related to the type of patch used; all 7 patients with an aneurysm were in the group in whom an isolated pericardial patch was placed ($p < 0.001$). In these patients, the mean RV pressure was 62.7 ± 17.1 mm Hg (range, 40 to 90 mm Hg), the mean RV/LV pressure ratio was 0.64 ± 0.2 (range, 0.40 to 1.00), and the mean Δp was 34.4 ± 16.5 mm Hg (range, 20 to 55 mm Hg).

Table 5. Clinical Factors Determining Fair or Unsatisfactory Results in 43 Patients in Late Follow-up

Results	Factor	No. of Patients[a]
Fair	RCD	14 (32.6)
	CTR	4 (9.3)
	Social handicap or postop complication	6 (14.0)
	RCD + CTR	4 (9.3)
	RCD + social handicap or postop complication	2 (4.7)
	CTR + social handicap or postop complication	1 (2.3)
Unsatisfactory	RCD requiring treatment (pacemaker, 2; medical therapy, 1)	3 (7.0)
	RCD + social handicap or postop complication	1 (2.3)
	RCD + CTR	1 (2.3)
	CTR + social handicap or postop complication	1 (2.3)
	RCD + CTR + social handicap or postop complication	1 (2.3)
	Reoperation + CTR	3 (7.0)
	Reoperation + CTR + RCD	2 (4.7)

[a] Numbers in parentheses are percentages.

CTR = cardiothoracic ratio ≥ 0.55; RCD = rhythm and conduction disturbance.

There have been five reoperations (3.3%), three for a residual VSD, one for subaortic stenosis, and one for residual stenosis of the pulmonary branches and coronary stenosis.

Some time after the operation, 1 patient (0.7%) died suddenly of unknown cause.

When the 43 patients with fair or unsatisfactory results were examined in terms of the type of residual defect, it was found that 16.3% (7) have major PI. However, when the patients with PI were considered separately, 53.8% (7/13) of them had a fair or unsatisfactory result (NS).

Eight (18.6%) of the 43 patients with a fair or unsatisfactory result had residual pulmonary stenosis (PS). However when the 24 patients with residual stenosis were analyzed separately, 8 (33.3%) showed fair or unsatisfactory results (NS). Also, 8 (18.6%) of the 43 patients with a fair or unsatisfactory result had a residual shunt, but 57.1% (8/14) of patients with a residual shunt had a fair or unsatisfactory result ($p < 0.05$).

Considering the various associations, 60.0% (6/10) of patients with a shunt and PS, 60.0% (3/5) of patients with a shunt and PI, 50.0% (2/4) of patients with PS and PI, and 66.7% (2/3) of patients with a shunt, PS, and PI had fair or unsatisfactory results.

The hemodynamic data showed that the highest mean RV pressure, RV/LV pressure ratio, and Δp (calculated over the entire RVOTO extending to peripheral branches) occurred in group 1, with nonsignificant variations in the other groups. Mean atrial pressure was mildly elevated in all groups, with the minimum in group 3 (subgroup with hypoplastic bifurcation) and the maximum in group 1 (see Table 4).

The mean protodiastolic and telediastolic pressures of the right ventricle in the three groups were, respectively, as follows: group 1, 0.5 ± 1.4 mm Hg and 9.6 ± 3.0 mm Hg; group 2, 0.05 ± 0.3 mm Hg and 9.7 ± 3.8 mm Hg; and group 3, 0.2 ± 1.0 mm Hg and 9.7 ± 3.0 mm Hg.

The RV diastolic pressures were mildly elevated in patients with major PI, revealing a degree of involvement of the right ventricle in all patients. The mean protodiastolic pressure was 0.2 ± 0.6 mm Hg (range, 0 to 2 mm Hg) and the mean telediastolic pressure was 10.1 ± 2.2 mm Hg (range, 6 to 11 mm Hg) in these patients.

The cardiothoracic ratio in these patients was 0.56 ±

Table 6. Early and Late Postoperative Cardiac Rhythm[a]

	Rhythm at End of CPB				Rhythm at Late Follow-up			
Group	Sinus	Other	Type[b]	No.	Sinus	Other	Type[b]	No.
1	14 (87.5)	2 (12.5)	Complete AV block	1	15 (93.8)	1 (6.3)	L ant. hemiblock + 1° AV block	1
			JR	1				
2	66 (88.0)	9 (12.0)	ST	1	58 (77.3)	17 (22.7)	AT + SVR	1
			Complete AV block	4			PVC	2
			1° AV block	2			ST	1
			JR	1			VT	1
			VT	1			1° AV block	3
							L ant. hemiblock	7
							JR	1
							WPM	1
3	53 (89.8)	6 (10.2)	Complete AV block	5	48 (81.4)	11 (18.6)	PVC	4
			ST	1			ST	2
							L ant. hemiblock	2
							Complete AV block	1
							LW	1
							1° AV block	1

[a] Numbers in parentheses are percentages. [b] This means the type of rhythm and conduction disturbance.

AT = atrial tachycardia; AV = atrioventricular; 1° = first-degree; JR = junctional rhythm; L ant. = left anterior; LW = Luciani Wencheback; PVC = premature ventricular contraction; ST = supraventricular tachycardia; SVR = slow ventricular rhythm; VT = ventricular tachycardia; WPM = wandering pacemaker.

0.1. The mean cardiothoracic ratio calculated for all 150 patients was 0.51 ± 0.05 ($p < 0.001$).

A reduction of the RV/LV pressure ratio from the early postoperative period to the first catheterization was noted in 65.4% (51/78); 3.8% (3/78) did not show any change; and 30.8% (24/78) had an increase. In the patients with a reduction, the mean global percent reduction was 23.29% ± 14.11%.

After the discontinuation of CPB, 88.7% of patients (133/150) were in sinus rhythm, and 11.3% (17) had rhythm or conduction disturbances. The disturbances included complete atrioventricular block in 58.8% (10/17), first-degree atrioventricular block in 11.8% (2), supraventricular tachycardia in 11.8% (2), junctional rhythm in 11.8% (2), and ventricular tachycardia in 5.9% (1) (Table 6).

Eight (47.1%) of the 17 patients with a rhythm or conduction disturbance in the early postoperative period acquired sinus rhythm. Twenty (15.0%) of the 133 patients in sinus rhythm after CPB had some disturbances later. In 9 (52.9%) of the 17 patients with a rhythm or conduction disturbance after CPB, the anomaly continued in the subsequent period ($p < 0.001$); it maintained the same characteristics in 55.6% (5/9) (NS). The evolution of the rhythm and conduction disturbances is summarized in Figure 1.

The late follow-up results in terms of these disturbances are shown in Table 6. In particular, we note the following:

The incidence of late rhythm and conduction disturbances was 19.3% (29/150).

Right bundle-branch block was found in 99.2% (120/121) of patients in sinus rhythm. It was complete in 97.5% (117/120) and partial in 2.5% (3/120) and was associated with left anterior hemiblock in 8.3% (10/120). Only 1 patient with a transannular patch had no conduction anomaly of the right or left branch.

Some treatment was necessary in 10.3% (3/29) of patients with a disturbance. It was medical in 1 patient with ventricular tachycardia and surgical (pacemaker implantation) in 2 for either third-degree atrioventricular block or slow junctional rhythm.

The patient who died, probably of an arrhythmia in the late postoperative period, a few months after a normally terminated pregnancy never showed a rhythm or conduction disturbance during routine checks.

Analysis and correlation of the fair and unsatisfactory results to the presumptive risk factors produced the following data:

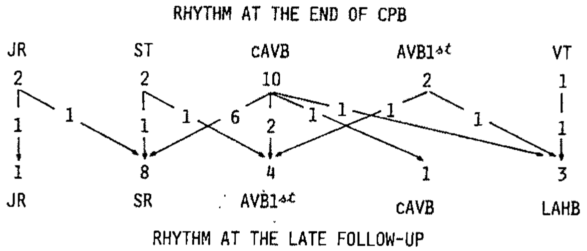

Fig 1. Evolution of the rhythm and conduction anomalies present at the end of cardiopulmonary bypass (CPB). (AVB1st = *first-degree atrioventricular block;* cAVB = *complete atrioventricular block;* JR = *junctional rhythm;* LAHB = *left anterior hemiblock;* SR = *sinus rhythm;* ST = *supraventricular tachycardia;* VT = *ventricular tachycardia.)*

Age: 10.0% (1/10) of the patients aged 5 years or younger, 25.0% (24/96) of patients between 5 and 10 years old, and 40.9% (18/44) of patients older than 10 years have fair or unsatisfactory results ($p \cong 0.05$).

Hematocrit: 69.8% (30/43) of patients with a fair or unsatisfactory result had a hematocrit of 50% or higher preoperatively, whereas 30.2% (13/43) had a hematocrit of less than 50% ($p < 0.05$).

Preoperative complications and associated anomalies: 14.0% (6/43) of patients with fair or unsatisfactory results had preoperative complications (NS), and 27.9% (12/43) had associated cardiac malformations (NS).

Palliation: 72.1% (31/43) had at least one shunt (NS).

Low output syndrome: treatment with substantial amounts of inotropic agents for longer than 24 hours in the early postoperative period was necessary in 20.9% (9/43) of patients with fair or unsatisfactory results; 9.3% (4/43) required only minimal inotropic support (NS).

Right ventricular pressure, Δp, RV/LV pressure ratio: the analysis of RV pressure and Δp (right ventricle–peripheral pulmonary artery) at the end of CPB (also if the absolute pressure was not very substantial because it was not correlated to the instantaneous output) revealed that 16.3% (7/43) (NS) of patients with fair or unsatisfactory results had an RV pressure greater than 50 mm Hg, and 14.0% (6/43) (NS) had a Δp greater than 30 mm Hg. The more reliable RV/LV pressure ratio was greater than 0.50 in 18.6% (8/43) (NS).

Comment

On the basis of these data, which are in accordance with those of others, we believe that repair of tetralogy of Fallot, although not strictly curative [1, 11, 12, 14], allows an almost normal life in terms of both survival and quality [1, 4, 12, 14, 15].

Our study provided the following data:

Of our patients, 96.0% (confidence interval [CI], 85%–100%; CI computed at 95%) are socially active, 92.0% (CI, 78%–100%) have good clinical exercise tolerance, and 79.3% (CI, 67%–93%) engage in sports activities.

The actuarial survival curve shows a survival of 100% at 8 years postoperatively and 99% at 17 years.

Right ventricular diastolic pressure shifts slightly but almost constantly from the normal range, and right atrial pressure mildly increases; the percentage of patients with an RV diastolic pressure of less than 0.6 mm Hg and a right atrial pressure of less than 5 mm Hg was, respectively, 9.0% (CI, 3.7%–17.6%) and 29.5% (CI, 19.7%–40.9%).

Rhythm and conduction disturbances are more frequent in our patients (19.3%; CI, 13.0%–26.0%) than in the general population.

The genesis of the mild but constant ventricular diastolic dysfunction is surely multifactorial. An important factor in the era preceding the use of cardioplegia may have been intermittent aortic cross-clamping.

In our correlation of fair and unsatisfactory results to the risk factors, age older than 10 years seems to be important and almost significant in increasing these results ($\chi^2 = 3.80$; $p \cong 0.05$). The role of polycythemia in the postoperative result is not certain, as it is impossible, in our opinion, to discriminate precisely the importance of polycythemia per se from the importance of the malformation determining the polycythemia. In our patients, associated cardiac malformations ($\chi^2 = 2.59$; $p =$ NS), preoperative complications ($\chi^2 = 0.52$; $p =$ NS), and low output syndrome ($\chi^2 = 0.05$; $p =$ NS) do not seem to play a significant role.

Our data confirm that the postoperative functional result, considering the optimal range of age, depends essentially on the surgical procedure and, in particular, on the presence and type of residual defects [1, 3–7, 10, 12, 14, 15]. Our correlation of the residual defects and the fair and unsatisfactory results demonstrated that residual shunts, although not hemodynamically important (mean shunt, 10.7% ± 6.6%), determine imperfect results. In fact, all of our patients with residual shunts (53.3%; CI, 26.6%–78.7%) later had a fair or unsatisfactory result ($\chi^2 = 4.68$; $p < 0.05$). On the other hand, the very small left-to-right shunts appearing in the early postoperative period show a tendency to disappear over time. For us, the transventricular approach and our technique of closure of the VSD allow a good view and, thus, a good chance of perfect closure, a good understanding of the infundibulum, and better preservation of the tricuspid valve.

In our clinical series, isolated residual stenosis seems to be better tolerated; only 33.3% (CI, 15.6%–55.3%) of the group with residual PS had fair or unsatisfactory results (NS). Nevertheless, the reconstruction of the RVOTO must be extended beyond the orifice of the left pulmonary artery. Also, the procedure demands particular attention regarding the choice of optimal diameter of the patch, as the risk of PI and minimal residual Δp (in our patients, mean $\Delta p = 36.8 \pm 11.3$ mm Hg) can very often determine the outcome. In our experience, stenosis of the bifurcation is not significantly associated with fair or unsatisfactory results provided the bifurcation is substantially enlarged.

In contrast to the conclusions of some authors [4, 6, 10–15] but in accordance with others [11, 12], our survey shows that substantial PI without residual Δp or pulmonary hypertension seems to be important to the postoperative result. In fact, 53.8% (CI, 25.1%–80.8%) of the group with PI had fair or unsatisfactory results. Minor PI seems to be well tolerated at the 11-year follow-up.

Various combinations of residual defects seem to be particularly relevant, even though they are not significant because of the small number of patients. Fifty percent of the patients with PI and PS, 60.0% of those with a VSD and PI, 60.0% with a VSD and PS, and 66.6% with PI, PS, and a VSD had fair or unsatisfactory results.

Aneurysms are a real risk to RV function [1, 4, 7, 16]. In our center, an aneurysm developed in 23.3% (CI, 9.9%–42.3%) of patients treated with an isolated pericardial patch, a very high number compared with the other kind of patch ($p < 0.001$). For this reason, at present, we reinforce pericardium with Dacron.

An objective, precise choice between the risk of residual PI and an elevated RV/LV pressure ratio is not easy. An elevated RV/LV pressure ratio at the end of bypass, in other groups [1, 5, 12, 13, 15] and in ours, constitutes a major risk factor for a fair or unsatisfactory result. Although our data, in accordance with those of others [1, 9, 15], confirm a reduction in RV/LV pressure ratio in the early postoperative period amounting to 23.3% ± 14.1% in 65.4% of patients with a further reduction predictable on the basis of nonproportional growth of the annulus and the pulmonary branches [16], the amount of reduction is not precisely predictable. Therefore, in our opinion, these data are not very reliable in terms of the individual patient.

Also, at present, PI has to be considered a major risk factor. The reports of late disturbances are more and more frequent, activity is reduced in these patients, RV diastolic pressure is increased, and ejection fraction is reduced both absolutely and as a response to effort [1, 11, 12, 17]. Cardiomegaly has to be considered a consequence of hemodynamic compensation with a tendency toward progressive worsening. A cardiothoracic ratio of 0.56 is present in 84.6% (CI, 54.5%–98.1%) of our patients with major PI; this is significantly different from the cardiothoracic ratio of 0.51 observed in the group of patients without PI ($t = 33.87$; $p < 0.001$).

On the basis of these two considerations, we use a transannular patch sized with reference to predicted diameters [16, 18] when the calculated RV/LV pressure ratio is greater than 0.60. We do not accept an intraoperative RV/LV pressure ratio greater than 0.60 if the stenosis is of the annulus, trunk, and branches, whereas we accept a ratio as great as 0.70 if the stenosis is only muscular/infundibular and if a good annulus and a competent valve are present.

Considering the greater chance to use a transannular patch in very young patients [1, 4, 6], even if we allow a reduction in age for repair [3, 7, 10], we agree with others [1, 5, 6, 12, 19, 20] that it is useful to palliate patients aged less than 6 months with a classic or modified (polytetrafluoroethylene) Blalock shunt. The simplicity of this operation, the efficacy of palliation, the low hospital mortality (approaching 0% in the best institutions [1, 4, 19]), the low mortality and morbidity in the intervening period, the simplicity of closure, and the near absence of hemodynamic complications favor this policy. The importance of a shunt on the final results in our patients is not significant ($\chi^2 = 0.002$). For these reasons, a Blalock shunt must not be considered an incremental risk factor. At present, aortopulmonary shunts, placement of more than one shunt, and an intervening period longer than 2 years between palliation and repair are not acceptable, in our opinion, except in the case of extreme hypoplasia or absence of growth of branches [1, 4, 6].

Rhythm disturbances and conduction abnormalities are by far the most frequent cause of fair or unsatisfactory results in our experience; 65.1% (CI, 49.1%–79.0%) of patients with such results have disturbances or abnormalities. Their appearance is a real risk intrinsic to the operation [1, 4, 11–15]. These arrhythmias can appear early or late [4, 13]. A late disturbance is not predictable solely on the basis of the type of rhythm after CPB, even if a greater incidence of rhythm and conduction disturbances can be presumed for patients who had some kind of arrhythmia in the immediate period after CPB; 52.9% (CI, 27.8%–77.0%) of our patients with disturbances after CPB had late disturbances ($\chi^2 = 11.56$; $p < 0.001$). Therefore, this behavior can be considered an incremental risk factor.

Left anterior hemiblock, the late appearance of which is perhaps related to fibrous reaction, and the moderate incidence of which is perhaps related to our type of closure of the VSD, has not, to date, created any particular problem in our patients and those of others [4, 12, 14]. Nevertheless, it must be considered a potential risk factor.

Particularly to be watched are patients in whom left anterior hemiblock is associated with a prolonged P-R interval and patients with complete atrioventricular block after the termination of CPB. The only patient with sudden late death, probably due to arrhythmias, was in sinus rhythm after CPB, had isolated right bundle-branch block, and had no other complaints during the routine checkups.

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Notice From the American Board of Thoracic Surgery

The American Board of Thoracic Surgery began its recertification process in 1984. Diplomates interested in participating in this examination should maintain a documented list of the cardiothoracic operations they performed during the year prior to application for recertification. They should also keep a record of their attendance at thoracic surgical meetings, and other continuing medical education activities, for the 2 years prior to application. A minimum of 100 hours of approved CME activity is required.

In place of a cognitive examination, candidates for recertification will be required to complete both the general thoracic and cardiac portions of the SESATS III syllabus (Self-Education/Self-Assessment in Thoracic Surgery). It is not necessary for candidates to purchase SESATS III booklets prior to applying for recertification. SESATS III booklets will be forwarded to candidates after their applications have been accepted.

Diplomates whose 10-year certificates will expire in 1991 may begin the recertification process in 1989. This new certificate will be dated 10 years from the time of expiration of the original certificate. Recertification is also open to any diplomate with an unlimited certificate and will in no way affect the validity of the original certificate.

The deadline for submission of applications is July 1, 1989. A recertification brochure outlining the rules and requirements for recertification in thoracic surgery is available upon request from the American Board of Thoracic Surgery, One Rotary Center, Suite 803, Evanston, IL 60201.

Björk-Shiley Strut Fracture and Disc Escape: Literature Review and a Method of Disc Retrieval

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Embolization of a prosthetic valve poppet is a rare but life-threatening event. It was reported sporadically before the introduction of the Björk-Shiley 70-degree convexoconcave prosthesis in 1980. Since that time, there have been a large number of reported mechanical failures with disc escape. The rate for the 29-mm to 33-mm mitral valves is estimated as 5.2%. In 29 of 35 patients (including the 2 presented here) in whom the site of disc lodgment could be determined, the disc was in the descending or abdominal aorta. Fifteen of these patients died. Six survivors had the disc removed at the same operation and 6 at a later operation. In 2 patients, the disc was not removed. In 2 patients in whom the disc was not removed initially, it was thought to contribute to postoperative complications. Two more cases of structural failure of the Björk-Shiley convexoconcave prosthesis are presented. A transpericardial approach to the descending aorta on bypass is described. It allows easy removal of the disc and eliminates the need for a second operation.

(Ann Thorac Surg 1989;47:436–40)

Mechanical failure of prosthetic heart valves with consequent escape of the poppet has been seen sporadically since the early days of valve replacement surgery [1–4]. The Björk-Shiley planar disc valve in its early models had failures of the weld of the inlet strut to the ring (5–7). Redesigning the valve to increase the cross-sectional area of the strut and eliminate the weld cured this problem.

The Björk-Shiley 60-degree convexoconcave valve, developed in 1976, had weld failures of the outlet strut, predominantly in the 29-mm to 33-mm mitral valves, which were withdrawn from the market in 1985 [8]. Failures have also been reported in aortic prostheses [9, 10].

The 70-degree opening-angle variant of the convexoconcave valve was introduced in 1980 and withdrawn from the market in 1983 because of the high incidence of outlet strut fractures. The risk of outlet strut fracture in this group has been estimated to be as high as 0.5% per year during the first 4 years after implantation [8]. As considerable numbers of patients have been exposed to the risk for less than 4 years, this will clearly be an ongoing problem.

Two cases of outlet strut fracture were seen in a 2-year period. In 1 of the patients, the retained disc caused problems in postoperative management. This led to the formulation of a strategy for management of the disc should the problem be seen again.

Material and Methods

Patient 1

A 57-year-old woman who had had two previous closed mitral valvotomies in 1953 and 1965 underwent mitral valve replacement in Switzerland in 1979. A Björk-Shiley convexoconcave valve was used. In 1983 she noted increasing shortness of breath and was admitted to another hospital. A diagnosis of valve thrombosis was made, catecholamine infusion was begun, and she was transferred to our hospital on November 28, 1983. On arrival she was in shock, anuric, and barely conscious. Chest roentgenograms showed severe pulmonary edema. Both valve struts appeared to be intact, but the disc could not be seen on the roentgenograms. Emergency operation was performed.

Femorofemoral bypass was established as the chest was opened. It was apparent that the disc was missing and that both struts seemed intact. The valve was excised without handling the outlet strut. When the outlet strut was touched with a forceps, it broke off immediately. The disc could not be seen or palpated in the heart or aorta. The mitral valve was replaced with a 33-mm Ionescu-Shiley valve, and bypass was discontinued without great difficulty.

A postoperative roentgenogram showed the disc at the level of the celiac axis in the abdominal aorta. Initial progress of the patient was good, and plans were made to recover the disk by laparotomy. However, before this could be accomplished the patient's condition deteriorated. Abdominal pain and distention with later diarrhea developed, and blood cultures grew *Staphylococcus aureus*. The sternotomy wound became infected, and the patient became anuric. Treatment with appropriate antibiotics and hemodialysis was begun, but her condition deteriorated rapidly and she died. Permission for an autopsy was refused.

Patient 2

A 59-year-old woman underwent mitral valve replacement (31-mm Björk-Shiley convexoconcave 60-degree valve) at another hospital in the Netherlands in 1982. She was well until the morning of September 20, 1985, when

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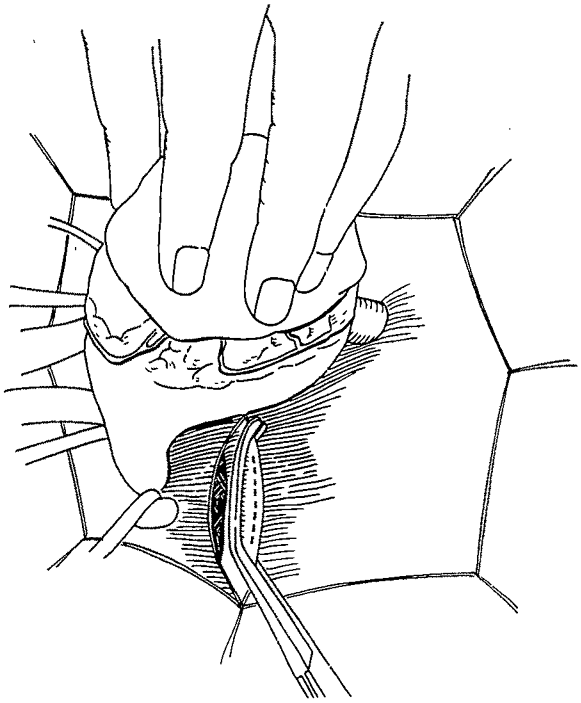

Fig 1. The heart is retracted cranially. The pericardium is opened posteriorly, and a clamp is placed on the descending aorta. The broken line shows the extent of the proposed incision.

she became acutely short of breath. She was examined in the local hospital, where a chest roentgenogram showed that the disc had escaped from the valve and was in the descending aorta at the level of the diaphragm. She was transferred for emergency reoperation.

The patient was taken directly to the operating room, and cardiopulmonary bypass was established. The valve was removed, and the strut was found in the right inferior pulmonary vein. The heart was retracted cranially, and the diaphragm was retracted caudally. An incision was made in the posterior aspect of the pericardium (Fig 1).

The descending aorta immediately above the diaphragm could be reached without difficulty. A Satinsky clamp was placed on the aorta, and an aortotomy was made. The ends were controlled with Prolene sutures (Fig 2), and the clamp was opened while perfusion was reduced to 500 mL/min. It was easily possible to manipulate the disc into a position where it could be grasped with a long forceps and removed. The aortotomy was then closed with the sutures.

After mitral valve re-replacement with a 31-mm Mitroflow prosthesis, bypass was discontinued with no great difficulty with the patient receiving a low-dose infusion of dopamine hydrochloride. The postoperative recovery was complicated by recurrent ventricular and supraventricular arrhythmias, but the patient was able to be discharged on the 14th postoperative day.

Comment

There is no doubt that the only appropriate treatment for mechanical failure of a prosthetic heart valve is immediate reoperation to replace the valve. This has been advocated since the earliest reported cases [1–4]. A vexing problem has been the management of an escaped occluder. If it is still in the heart, there is little difficulty, but when it has migrated out of reach, there is some dispute as to the appropriate management.

The problem of occluder escape has been seen sporadically in many types of valve over the years: Wada-Cutter [3], Smeloff-Cutter [2], Cooley-Cutter [4], Björk-Shiley Delrin disc [1], and Björk-Shiley spherical disc [5–7]. However, since the introduction of the Björk-Shiley convexoconcave valves, both the 60-degree and 70-degree models (in 1979 and 1980, respectively), a large number of mechanical failures, with consequent disc escape, have been reported. In response, the 70-degree valve was completely withdrawn in 1983, and the 60-degree valve in sizes 29-mm to 33-mm was withdrawn in 1985 [8].

By 1985, an estimated 80,000 convexoconcave valves had been inserted [10], 4,028 of them the 70-degree model [8]. Consequently, in spite of the recalls, a considerable number of the valves are at risk. In addition, the problem has not been absent from 60-degree valves less than 29-mm in size [11], and a number of failures have now been reported in 27-mm valves [12–16]. In their series of 113 valves processed after March 1, 1982, Mok and associates [15] found a fracture rate of 3.5%.

A computer search of the English-language literature located a considerable number of cases in which the site of final disc lodgment and the way in which it was managed were reported in sufficient detail to allow tabulation (Table 1). The great majority (29/35 or 83%) of discs were found in the descending thoracic or abdominal aorta. If one considers only patients with a Björk-Shiley convexoconcave valve, 13 (59%) of 22 patients died, 6 before, 3

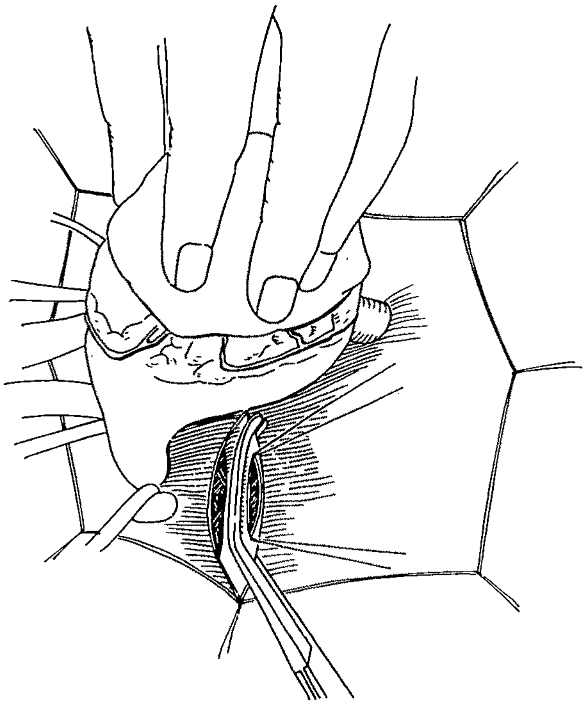

Fig 2. The aorta has been incised, and stay sutures have been placed prior to removal of the clamp.

Table 1. Summary of Data on Patients with Disc Lodgment and Its Management

Reference	Year	Age (yr)	Valve	Size (mm)	Time to Failure (mo)	Reoperation	Outcome	Disc Site	Disc Removed	Removal Delay
Messmer et al [1]	1973	...	B-S D	31 Mitral	18 h	Yes	Died later	Descending aorta	No	...
Keen [2]	1974	...	S-C	Mitral	72	No	Died before reoperation	Aortic arch	...	...
Hughes et al [3]	1975	49	W-C	28 Mitral	61	Yes	Survived	Abdominal aorta	Laparotomy	Same operation
Ansboro et al [4]	1976	55	C-C	Mitral	6	Yes	Survived	Abdominal aorta	Laparotomy	2 mo
McEnany et al [5]	1979	25	B-S s	29 Mitral	7	Yes	Survived	Left atrium	...	Same operation
Larrieu et al [6]	1982	22	B-S s	31 Mitral	72	Yes	Survived	Abdominal aorta	Laparotomy	2 mo
Dubernet et al [7]	1986	40	B-S s	29 Mitral	3 h	Yes	Survived	Abdominal aorta	No	...
		54	B-S s	29 Mitral	72	Yes	Survived	Abdominal aorta	No	...
Jaumin et al [9]	1984	45	B-S cc 60	23 Aortic	24	No	Died before reoperation	Abdominal aorta	...	...
Lifschultz and Donoghue [10]	1985	35	B-S cc 60	29 Aortic	16	No	Died before reoperation	Abdominal aorta	...	...
Ibarra et al [11]	1984	44	B-S cc 60	31 Mitral	10	Yes	Survived	Left ventricle	...	Same operation
Garcia-del-Castillo et al [12]	1985	55	B-S cc 70	27 Mitral	9	Yes	Survived	Abdominal aorta	Laparotomy	4 days
Miccolo et al [13]	1985	34	B-S cc	27 Mitral	28	Yes	Died during reoperation	Abdominal aorta	No	...
Goovaerts and De Geest [14]	1986	46	B-S cc 60	27 Mitral	44	Yes	Died during reoperation	Abdominal aorta	No	...
		55	B-S cc 60	27 Mitral	5	No	Died before operation	Left ventricle	...	...
Mok et al [15]	1985	31	B-S cc	29 Mitral	9	No	Died before reoperation	Descending aorta	...	...
		47	B-S cc	Mitral	26	No	Died before reoperation	Abdominal aorta	...	...
		20	B-S cc	31 Mitral	8	Yes	Survived	Descending aorta	Laparotomy	1 day
		14	B-S cc	27 Mitral	17	Yes	Survived	Descending aorta	Laparotomy	Not given
		32	B-S cc	29 Mitral	23	Yes	Died later	Descending aorta	No, too sick	...
Nakano et al [16]	1986	42	B-S cc	27 Mitral	21	Yes	Survived	Abdominal aorta	Laparotomy	Same operation
Norenberg et al [17]	1977	...	B-S s	31 Mitral	7	No	Died before reoperation	Abdominal aorta	...	...
Ninomiya et al [18]	1983	61	B-S cc 60	31 Mitral	2	Yes	Died later	Abdominal aorta	No	...

Table 1. Continued

Reference	Year	Age (yr)	Valve	Size (mm)	Time to Failure (mo)	Reoperation	Outcome	Disc Site	Disc Removed	Removal Delay
Sethia et al [19]	1983	36	B-S cc	31 Mitral	9	Yes	Survived	Abdominal aorta	Laparotomy	5 days
		...	B-S cc	Mitral	10	Yes	Died later	Abdominal aorta	No	...
Fennerty et al [20]	1984	45	B-S cc	Mitral	37	No	Died before reoperation	Aortic arch	...	...
Goerttler and Kaiser-Martini [21]	1984	56	B-S cc	Mitral	3	No	Died before reoperation	Abdominal aorta	...	...
		54	B-S cc	Mitral	25	No	Died before reoperation	Abnominal aorta	...	...
Sacks et al [22]	1984	52	B-S cc 60	29 Mitral	12	Yes	Died during reoperation	Left ventricle	...	Same operation
Casarotto et al [23]	1985	...	B-S cc	Mitral		Yes	Died during reoperation	Descending aorta	No	...
Davis et al [24]	1985	21	B-S cc	29 Mitral	10	Yes	Survived	Abdominal aorta	Laparotomy	Same operation
Khalil et al [25]	1985	44	B-S cc	31 Mitral	<24	Yes	Survived	Abdominal aorta	Laparotomy	Same operation
McGeehin et al [26]	1986	46	B-S cc	Mitral	48	Yes	Survived	Abdominal aorta	Laparotomy	Same operation
Hendel [present report]	1989	57	B-S cc 60	29 Mitral	48	Yes	Died later	Abdominal aorta	No	...
		59	B-S cc 60	31 Mitral	36	Yes	Survived	Abdominal aorta	New approach	Same operation

B-S = Björk-Shiley; cc = convexoconcave; C-C = Cooley-Cutter; D = Delrin; s = spherical; S-C = Smeloff-Cutter; W-C = Wada-Cutter.

during, and 4 after reoperation. Of the 9 survivors, 5 underwent removal of disc during the same operation [16, 24–26, present report (patient 2)]. The remaining 5 had a laparotomy at times ranging from one day [15] to 1 month [6].

In 2 patients who had failure of Björk-Shiley spherical-disc valves, the disc was left in situ in the abdominal aorta. The patients were alive and well and experiencing no problems from the discs at 8 years and 1 year when reported [7]. Nevertheless, the potential exists for long-term problems related to erosion, infection, or thrombosis at the site of disc lodgment.

In the patient of Larrieu and associates [6] and patient 1 reported here, the disc may have contributed to postoperative problems. The patient of Larrieu and co-workers experienced recurrent bloody diarrhea, which did not clear completely until the disc was removed at 1 month. In our patient 1, the first of the postoperative problems was also abdominal. The hypothesis that the presence of the disc in the abdominal aorta, partially occluding the celiac axis, caused intestinal ischemia is difficult to prove but impossible to discount.

When others [4, 6, 19, 25] have made specific comment about the management of the disc, they have thought that eventual removal was mandatory. Opinion is divided about the timing of removal; some [3, 16, 24–26] remove the disc at the same operation, and others advocate waiting until the patient's condition is stable [6, 15, 19]. In one instance, the patient was stated to be too sick to undergo a further procedure at the end of cardiopulmonary bypass [15].

In conclusion, the technique described (patient 2) avoids the need for a separate laparotomy in patients whose condition is too unstable or who are simply too sick to undergo such a procedure. In addition, it saves the patient the need for later anesthesia and laparotomy with the attendant risks and prolongation of hospital stay. The approach to the descending aorta after removal of the failed valve but before insertion of the new valve allows easy retraction of the heart upward and provides excellent exposure. It would have been easy to pass a Fogarty catheter in either direction, as done by Hughes and co-workers [3], to retrieve an occluder that was beyond direct reach. This technique allows the removal of one factor that may cause considerable uncertainty in the postoperative management of patients with an already difficult problem.

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Thermal Coronary Angiography: A Method for Assessing Graft Patency and Coronary Anatomy in Coronary Bypass Surgery

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Thermal coronary angiography was evaluated in 50 patients undergoing 137 saphenous vein and 48 internal mammary artery bypass grafts. A total of 177 thermal coronary angiograms were performed after completion of the distal anastomoses by injection of cold cardioplegia into the vein or by reperfusion with warmer blood in the internal mammary artery grafts. These angiograms provided details of graft and anastomosis patency, flow directions, and presence of native coronary stenoses. Temperature differences between the injectant and the epimyocardium of greater than 4°C resulted in high-contrast images. Thermal coronary angiograms were obtained in 173 of the 177 studied bypass grafts; 172 grafts were patent, and 1 internal mammary artery graft was occluded. Unsuspected stenoses were detected at the site of four distal anastomoses. Subsequently, two anastomoses were successfully revised and three additional grafts performed. Ninety-six native coronary stenoses were located in the recipient coronary arteries. In ten instances, the thermal coronary angiograms were obscured by excess fat or myocardium, thereby impeding correct image analysis. We conclude that thermal coronary angiography can be clinically relevant and helps improve decision making during coronary artery bypass operations.

(Ann Thorac Surg 1989;47:441–9)

Thermography is a technique for recording, in color-coded images, small temperature differences between adjacent structures. Modern infrared imaging systems consist of a scanning thermal camera, a video monitor, and a videotape recorder. Infrared radiation is detected and quantitated by special heat detectors in the scanner; it is then transformed to an electrical signal and displayed as a thermal image on a monitor. Recent technical advances in thermographic imaging have led to the development of systems that are more accurate, can be linked to digital image processors, and therefore are suitable for operating room use.

Although thermography has been used to measure the cooling effects of cardioplegic solutions [1–3] and to assess coronary perfusion in subtended myocardial segments [4–8], it has never been applied as a routine clinical tool during cardiac operations because the images have not been sufficiently precise to be useful. Instead, assessment of intraoperative graft patency is either assumed or based on passage of coronary probes, electromagnetic flow measurements, or, most recently, angioscopy [9, 10]. Each of these methods, however, has important limitations in operating room use.

The goal of this feasibility study was to evaluate thermography as a method for performing intraoperative coronary angiography during "usual" coronary procedures, to further refine such technology to this end, and to determine whether such studies may be of clinical value.

Material and Methods

Patient Population

In a randomly chosen population of 37 male and 13 female patients undergoing coronary artery bypass grafting, intraoperative thermographic imaging of the graft, the bypassed native coronary artery, and the perfused epimyocardial segment of the heart was performed. Mean age of the patients was 65.7 years (range, 34 to 88 years). Thirty-eight patients had severe three-vessel disease, and 12 had one-vessel or two-vessel disease; in 9 patients, the distal coronary arteries were diffusely diseased. Twenty-one patients had stable angina and 18, unstable angina. The remaining 11 patients were experiencing acute infarctions: 5 of them had had prior myocardial infarctions. An additional 11 patients also had had remote infarctions. Thus, 22 patients had sustained one or more acute or remote myocardial infarctions at the time of this operation. Four patients had previously been operated on because of coronary artery disease. The 50 patients received a total of 185 bypass grafts, 48 internal mammary artery (IMA) and 137 saphenous vein (SV) grafts, an average of 3.7 grafts per patient. Five aortic valves and one mitral valve were replaced as well.

In agreement with the chairman of the Human Use Committee at Cedars-Sinai Medical Center, to whom this

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project was presented before clinical application, patient consent for each single study was not necessary, as the use of thermography has been approved by the Food and Drug Administration for clinical application. Furthermore, there was no direct contact between the equipment and the patient, and there was no interference with the conduct of or alteration in technique of the operation performed during these studies.

Technique of Thermal Coronary Angiography

A liquid nitrogen–cooled 782 Agema (AGA) thermal camera (Agema Infrared Systems AB, Danderyd, Sweden) with a 7-degree lens was used for the first 25 patients, and an advanced version, an electronically cooled 870 AGA camera with a 12-degree lens, was used in the second 25 patients. Aside from improved image quality, there were no apparent differences in the nature of the data obtained with one or the other camera; therefore, the results were pooled for further analyses. Both cameras were mounted on a tripod and focused directly on the exposed surface of the heart at a distance of 1 m. The optimal angle for the camera was perpendicular (90 degrees) to the heart surface. In practice, however, tilting the 782 AGA camera was limited to a camera angulation of 70 to 80 degrees. The camera settings were adjusted by the operator to the expected temperatures; the settings were 20°C for the SV and 30°C for the IMA grafts with a range of ±10°C. Both camera systems provide a maximum spatial resolution of 0.1 to 0.2 mm and a thermal resolution of 0.6° to 0.8°C under these conditions.

The images were displayed either in black and white or in color on a high-resolution monitor in real time. Each color or gray-scale level represented an isotherm. Selected images were enhanced and analyzed in real time using the attached TIC 8000 image processor; the final images from each patient study were stored on floppy diskettes. Thermal coronary angiograms were obtained after completion of the distal anastomoses by injection of 30 mL of cold (8° to 14°C) crystalloid cardioplegia into the proximal vein grafts or by perfusion with warmer (25° to 30°C) blood after removing the bulldog clamp from the IMA grafts. As these are the routine methods for infusing supplemental cardioplegia and for checking anastomoses for patency or leaks, thermal coronary angiography (TCA) required only optimal exposure of the heart and focusing of the camera on the area of interest. The difference between the injectant and the epicardial temperatures allowed us to delineate the graft and native coronary anatomy.

Thermal coronary angiograms were used to evaluate graft patency, the character of anastomotic sites, native coronary anatomy including stenoses, flow directions, and regions of distal epimyocardial perfusion. Direction of flow was classified as anterograde or retrograde, and perfusion of branches and collaterals was established. Each of these observations was graded subjectively from 0 through 3, representing no flow to optimal flow. Regional perfusion distal to each graft was assessed using the image processor; this was quantified by calculating the area of induced epimyocardial temperature change. Results of TCA were compared with intraoperative coronary probe calibrations and with the preoperative cineangiograms of the coronary arteries. Cineangiograms and catheterization reports were not reviewed until after the thermal coronary angiogram was analyzed.

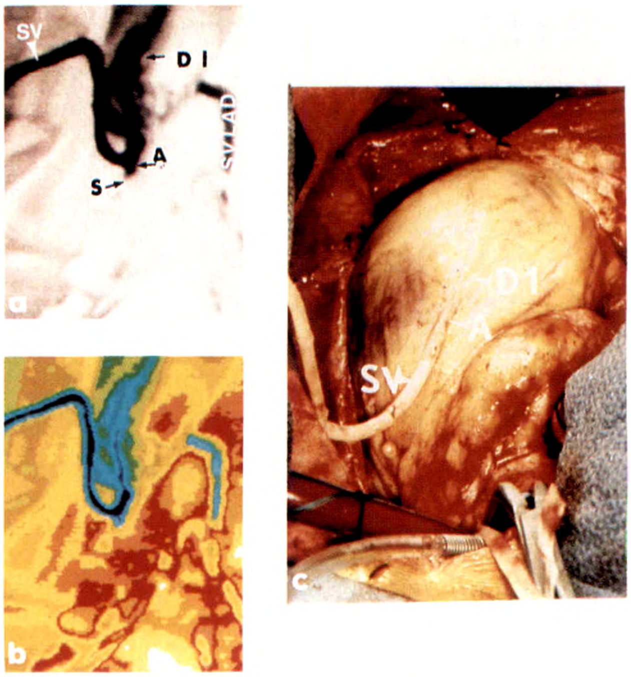

Fig 1. Thermal coronary angiogram of saphenous vein graft (SV) anastomosed to the first diagonal (D1). The anastomotic site is marked by an arrow (A). (a) Real-time thermal coronary angiogram in black and white and (b) in color. Retrograde flow is obstructed by a high-grade intracoronary stenosis (S). A left anterior descending coronary artery saphenous vein graft filled by small collaterals is also detected by thermal coronary angiography. (c) Operative field on which the thermal camera focuses. This is a left anterior descending coronary artery vein graft to the first diagonal artery.

Each real-time thermal coronary angiogram was graded 1 through 3 for image quality before image enhancement. These results were later correlated to camera angle, injectate–epicardial temperature difference, and the presence of fat or muscle covering the coronary arteries.

Data were entered in a specially designed spreadsheet (data base) developed on SYMPHONY software (Lotus Inc). The spreadsheet allowed complete intraoperative data storage and provided continuous updating, evaluation, and statistical analysis of the data. This program was also installed on the same computer used to process images.

Results

Illustrative Examples

Figure 1 shows the view of the operative field (1c), as well as a typical thermal coronary angiogram of an SV graft (1a, 1b). The bypass graft is anastomosed to a first diagonal coronary artery. The vein graft and the coronary artery are delineated by the temperature difference between the injected cold cardioplegia (<13°C) and the epicardial temperature (>28°C). Figure 1a shows the real-time thermal coronary angiogram in black and white; the image reveals an optimal distal graft anastomosis and unimpeded anterograde runoff. Retrograde flow stops abruptly 1 cm proximal to the anastomosis, where flow is obstructed by a high-grade intracoronary stenosis. The left anterior descending coronary artery (LAD) SV graft is filled by collaterals. The colder areas are displayed in dark gray or black according to the corresponding temperatures/isotherms. Figure 1b shows the same image in the real-time color mode without image enhancement.

Figure 2a shows an IMA graft. The bypass graft is anastomosed to a first circumflex marginal coronary artery. In this image, both the bypass graft and the recipient vessel are white because the injected subclavian artery blood at 29°C perfuses the epimyocardium at 23°C. The image can be inverted (Fig 2b) to obtain an appearance similar to the SV thermal angiogram. The distal anastomosis is unremarkable, and the IMA graft provides good anterograde flow; the second marginal branch is also perfused through small collaterals. Retrograde flow is diminished, and there is a native coronary stenosis proximal to the IMA graft anastomosis, which was confirmed by intraoperative calibration with a probe and preoperative cineangiography (Fig 2c).

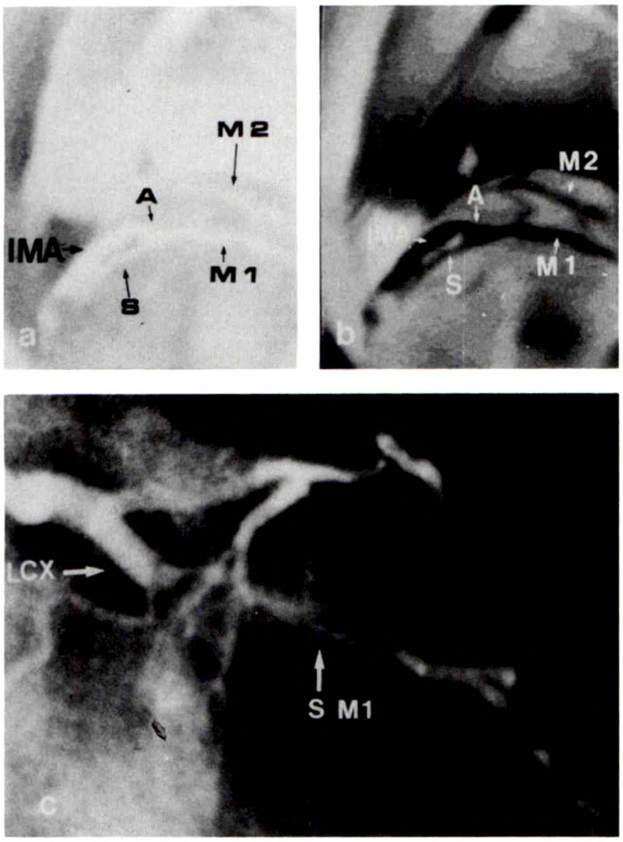

Fig 2. Thermal coronary angiogram of patent internal mammary artery graft (IMA) anastomosed on the posterolateral left ventricle to the first circumflex marginal (M1). (a) Real-time black and white mode and (b) inverted black and white mode. The circumflex marginal coronary artery, the graft, and the distal anastomosis (A) are clearly visible. (c) The corresponding cineangiogram reveals a severe segmental stenosis (S) of the first left circumflex marginal (LCX), which was delineated by thermal coronary angiography as well. (M2 = second marginal branch.)

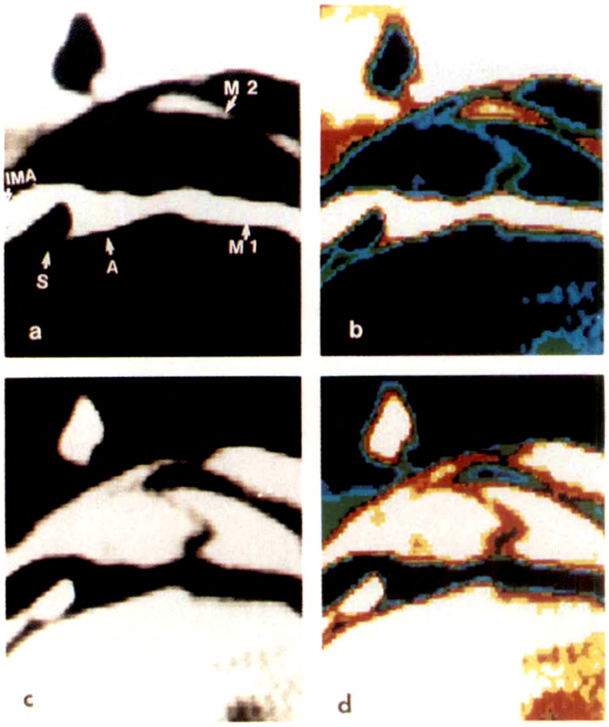

Fig 3. Thermal coronary angiogram of internal mammary artery graft (IMA) enhanced by image processing (1 × high pass, 1 × low pass filter and temperature scaling) in (a, c) black and white and (b, d) color. Images are displayed in both normal mode (a, b) and inverted mode (c, d). The color pictures depict the anastomotic site (A), the coronary anatomy (M1 [circumflex marginal], M2 [second circumflex marginal]), and the proximal native coronary stenosis (S) in greater detail.

Figure 3 demonstrates the use of image enhancement using the TIC 8000 thermal image computer (Agema). The images were contrast enhanced, filtered, and magnified in black and white and in color. Contrast was enhanced using a nonlinear thermal scale, thereby allowing enhancement of selected temperatures. In these IMA thermal coronary angiograms, the temperature scale from 26° to 29°C was enhanced in reference to the blood temperature of 28°C, and then enhancement of the lower temperature range from 13.9° to 24.4°C was used to create a high-contrast image and a uniform background. These images demonstrate the potential of image processing in TCA using the same image of the IMA graft shown in Figure 2. Magnification and scaling commands enhanced these images in normal and inverted mode in black and white and in color.

Efficacy of Thermal Angiography

Thermal coronary angiographic studies were performed in 177 of the 185 bypass grafts; for logistical reasons, eight grafts were not studied. Four of the 177 were not imaged because of low temperature differentials between the

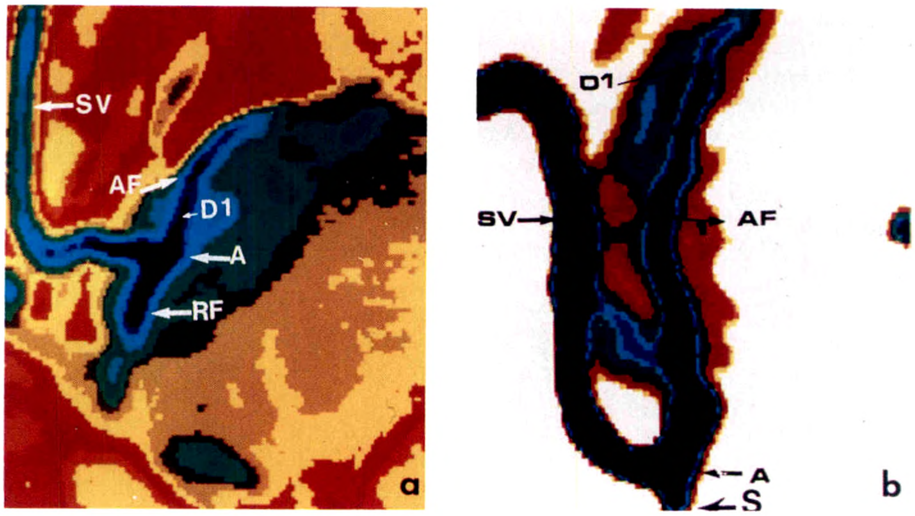

Fig 4. Thermal coronary angiograms of anastomosis (A) saphenous vein grafts (SV) to the first diagonal coronary arteries (D1) demonstrating (a) optimal anterograde (AF) and retrograde (RF) flow and (b) only anterograde flow. These angiographic findings are confirmed by the regional epicardial perfusion fields from the anastomosis, as quantitated by the induced temperature distribution: (a) distal and proximal myocardial perfusion (green areas) versus (b) distal perfusion only (red and green areas). (S = stenosis.)

injectant and the epimyocardium. Of the 173 grafts imaged, 172 demonstrated graft patency; only one IMA graft to the LAD was found to be occluded within the IMA proximal to the anastomotic site. The surgical procedure was altered on the basis of this datum, and a second patent vein graft was placed distal to the IMA anastomosis. Thus the success rate for patency of the bypass grafts was 99.4%.

Detection of Stenoses in Bypass Grafts and Native Coronary Arteries

In addition to validating graft patency, examination of the thermal coronary angiograms provided an opportunity to determine whether there were anastomotic or coronary artery stenoses in proximity to the anastomoses. Fourteen areas of stenosis at the site of anastomoses were identified, seven at the toe and five at the heel of the anastomoses. In one instance there were both proximal and distal stenoses. Four of these anastomotic stenoses were unsuspected. Twelve of the 14 were related to diffuse disease in the native coronary arteries, and the surgical procedure was therefore not changed. In the remaining two instances, the native coronary arteries were normal at the anastomotic site, and these anastomoses were successfully revised. Anastomotic stenoses most frequently occurred in circumflex marginal or right posterior descending coronary artery anastomoses. In two IMA–LAD grafts, anastomotic stenoses were detected at the proximal heel.

In the 173 imaged native coronary arteries, 96 stenoses were detected. Sixteen were distal and 80 were just proximal to the anastomoses. These findings were confirmed with TCA in 94 of the 96 cases. Only two of the 16 distal stenoses detected by TCA were unsuspected, and one of these was managed by performing an additional distal graft. In the other cases, severe diffuse distal artery disease accounted for the finding, and the situation did not allow for further operative improvements. Thermal coronary angiography detected every distal coronary stenosis that was seen in the preoperative cineangiographic studies. Further, TCA delineated two unsuspected proximal coronary stenoses in totally occluded arteries, which were poorly filled by collaterals in the preoperative cineangiogram. Because the more proximal left coronary artery and the right coronary artery are obscured by the aorta and the pulmonary artery, and therefore are not imaged by TCA, only 80 of the 157 proximal cineangiographic stenoses were detected by TCA. Inability to assess the proximal lesion was equally true when calibration was attempted with probes, and, in fact, most proximal stenoses are not detectable by evaluations made from the coronary arteriotomy site.

Assessment of Anterograde and Retrograde Flow

Figure 4a shows an SV graft with optimal anterograde and retrograde flow. In contrast, Figure 4b shows only anterograde flow because retrograde flow is prevented by total obstruction of the proximal native coronary artery. The epimyocardial areas of graft perfusion were determined as areas of temperature change after TCA and correspond to what would be expected from the coronary anatomy.

In this study, 88% of the grafts were graded as having excellent anterograde flow, but only 36% of the grafts had excellent retrograde flow. Twenty grafts had reduced anterograde flow, which correlated with distal anastomotic and coronary artery stenoses. Of the 110 grafts (64%) with reduced retrograde flow, 6 had proximal anastomotic heel stenoses and 80 had proximal native coronary stenoses. In contrast, optimal anterograde and retrograde flow from the anastomosis was observed in all normal arteries and normal anastomotic sites. Thus, the presence of intracoronary stenoses correlated with and had a major influence on bypass graft flow direction and epimyocardial perfusion areas. Twenty-seven percent of all grafts provided perfusion through collaterals to other coronary arteries. Collateral perfusion was limited, in general, in grafts with proximal and distal stenoses.

Influence of Thermal Coronary Angiography on Intraoperative Decision Making

In this study, intraoperative decision making was affected in two ways: either this information was used as the basis

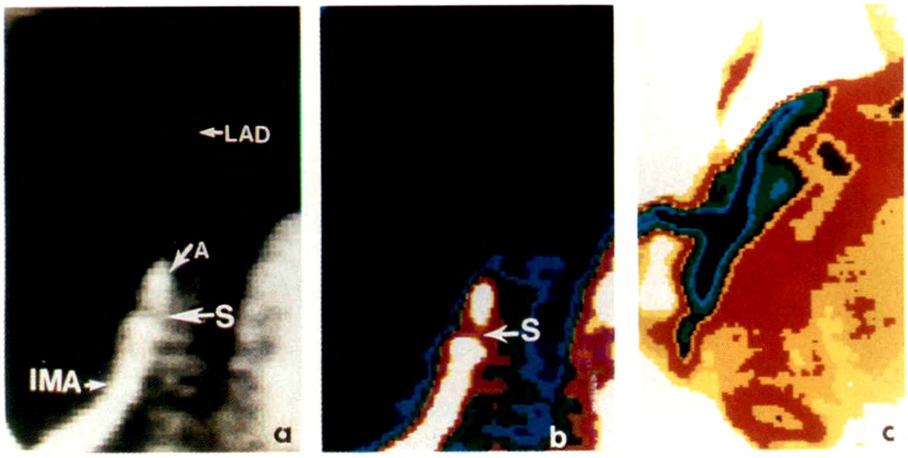

Fig 5. Thermal coronary angiogram showing occlusion in internal mammary artery graft (IMA) itself. This occlusion was unsuspected and was detected by thermal coronary angiography, which revealed a lack of perfusion at the anastomotic site (A) and into the native coronary bed (LAD [left anterior descending coronary artery]). The superiority of the color-enhanced mode (b) is clearly illustrated by contrasting it with the black and white mode (a). (c) Subsequently performed distal vein graft. (S = stenosis.)

for making a decision to revise a graft or it was used to influence the number of grafts placed. Figure 5 demonstrates how TCA led to placement of an additional graft. The image shows an obstructed IMA–LAD graft in which flow of warmed blood occurred within the IMA only to within 1 cm proximal to the anastomosis. When an additional distal vein graft to the LAD was subsequently placed (Fig 5c), the location of this obstruction in the IMA was confirmed by retrograde passage of coronary probes. This case also illustrates the fact that the color-enhanced image (Fig 5b) is more revealing than the black and white image (Fig 5a).

Figure 6 demonstrates the discovery of an unsuspected stenosis. The image shows an SV graft to the first circumflex marginal. The unsuspected stenosis was discovered at the distal tip of the anastomosis. On the basis of this finding the anastomosis was revised, and a dissected plaque was noted to have caused the obstruction. After revision, repeat TCA (Fig 6c) demonstrated the success of the surgical alteration.

Figure 7 illustrates how the findings of TCA contributed to the decision to place 1 rather than 2 grafts. The LAD vein graft anastomosis was placed close to the origin of the first diagonal. Thermal coronary angiography documents that both the LAD and its diagonal branch are well perfused by the single graft, thereby eliminating the need for a separate diagonal graft.

In the 173 grafts imaged, there were nine instances in which the availability of TCA contributed to decision making. These nine instances included five graft revisions (placement of three additional grafts and revision of two anastomoses). In two other cases, a graft that was thought necessary preoperatively was shown to be superfluous. In two additional cases in which TCA revealed unexpected tight stenoses at the anastomotic site, the grafts were not revised because the native arteries were too severely diseased to allow a more effective anastomosis at that site or elsewhere. These nine instances occurred in 8 of the 50 patients studied.

Limitations of Thermal Coronary Angiography

Thermal coronary angiography did not provide information about the most proximal parts of the left coronary artery, i.e., those portions covered by the aorta and the pulmonary artery or invisible behind the heart. Imaging bypass grafts on the posterolateral left ventricular wall in the distribution of the circumflex marginals required extensive tilting of the scanning camera but no extraordinary exposure. In the first 25 patients for whom the AGA 782 camera was used, impaired image quality of posterior

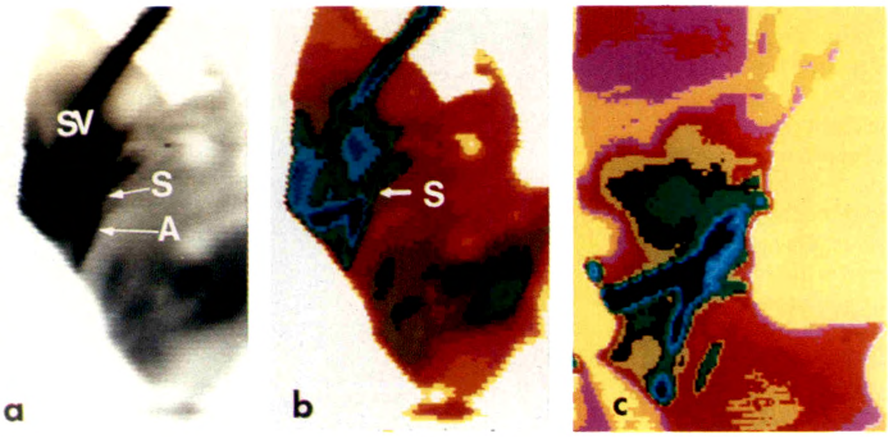

Fig 6. Example of stenosis (S) at the distal toe of a saphenous vein graft (SV) anastomosis. The narrowing (A) is clearly seen in (a) black and white and (b) color. (c) After revision of this anastomosis, the subsequent thermal coronary angiogram documents the improved result not only angiographically but also by virtue of the increased area of epimyocardial perfusion.

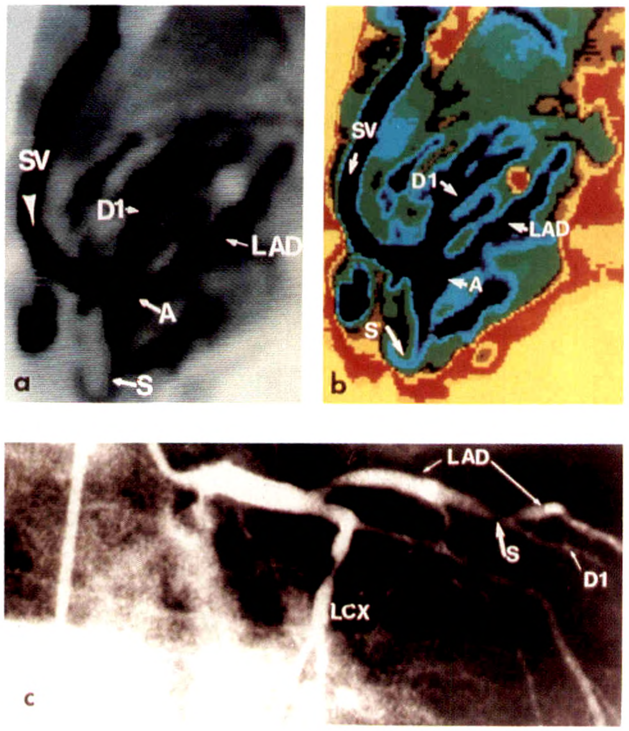

Fig 7. Thermal coronary angiogram in (a) black and white and (b) color documents excellent simultaneous perfusion of the diagonal branches (D1) *and the left anterior descending coronary artery* (LAD) *by a single saphenous vein graft* (SV)*. The obstruction in the left anterior descending coronary artery* (S) *is clearly shown not to affect the origin of the first diagonal and amplifies the findings of the preoperative coronary angiogram (c).* (LCX = *left circumflex marginal.)*

and inferior wall vessels occurred in 23 of 43 circumflex and right thermal coronary angiograms. In the second cohort of 25 patients for whom the electronically cooled thermal camera was used, only six of the 40 thermal coronary angiographic images were impaired.

It was also found that when extensive epicardial fat or a muscle bridge covers the coronary arteries, image quality is compromised. Figure 8 is an example of TCA of a vein graft to the first circumflex marginal; discontinuity was seen beyond the anastomosis in the distal coronary artery. The suspected stenosis was found to be a thick myocardial bridge. Muscle bridges occurred in 13 patients, most frequently involving the circumflex marginal branches. Extensive pericoronary adipose tissue compromised image quality 14 times: in the LAD grafts, seven times; the proximal right coronary artery grafts, five times; and the diagonal grafts, twice.

Rarely, images were spoiled by leaks at the anastomotic site. Figure 9 shows a thermal coronary angiogram spoiled by an anastomotic leak, and depicts the same graft before (Fig 9a) and after (Fig 9b) repair of the anastomotic leak. Figure 9b indicates that this leak was controlled without compromising the integrity of the anastomosis, and delineates precisely the coronary anatomy.

Several other technical constraints were also demonstrated. High-contrast images are a function of the temperature gradient between the injectant and the epimyocardium. This gradient optimally should be greater than 4°C. In the 4 patients in whom the temperature gradient was less than 0.8°C, no image was obtained. At these camera settings, this temperature differential proved to be the minimum gradient necessary for contrasting the grafts and coronary arteries by TCA. In each of the 12 patients with temperature differentials of less than 3°C, enhancement was required before evaluation. The thermal coronary angiograms could also be compromised by camera angle and by leaks. A second injection after repair of a leak often corrected the latter drawback.

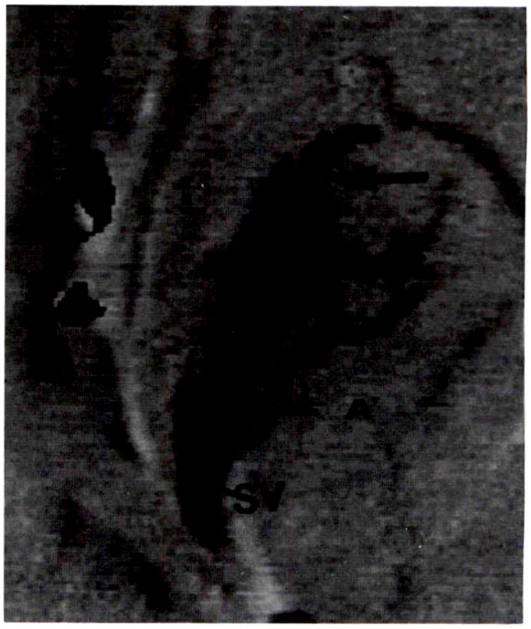

Fig 8. Thermal coronary angiogram of a saphenous vein graft (SV) *to the first circumflex marginal* (M1) *reveals a distal discontinuity* (arrow)*, which was caused by a myocardial bridge at this level of the coronary artery.* (A = *anastomosis.)*

Table 1 summarizes all of these limitations noted in the 177 thermal coronary angiograms and documents how often image analysis was affected.

Real-time image quality varied with graft location. On our 0 through 3 ordinal scale, image quality averaged 2.6 for the first diagonal, 2.3 for the LAD, the proximal right,

Table 1. Summary of Recognized Limitations During 177 Real-Time Thermal Coronary Angiographic Studies and Influence on Image Quality

Limitation	Problematic Thermal Coronary Angiograms	Possible Evaluation	Impossible Evaluation
Temperature difference	16	12	4
Camera angle	29	22	7
Fat	14	9	5
Muscle	13	8	5
Leaks	9	7	2
Total	81	58	23

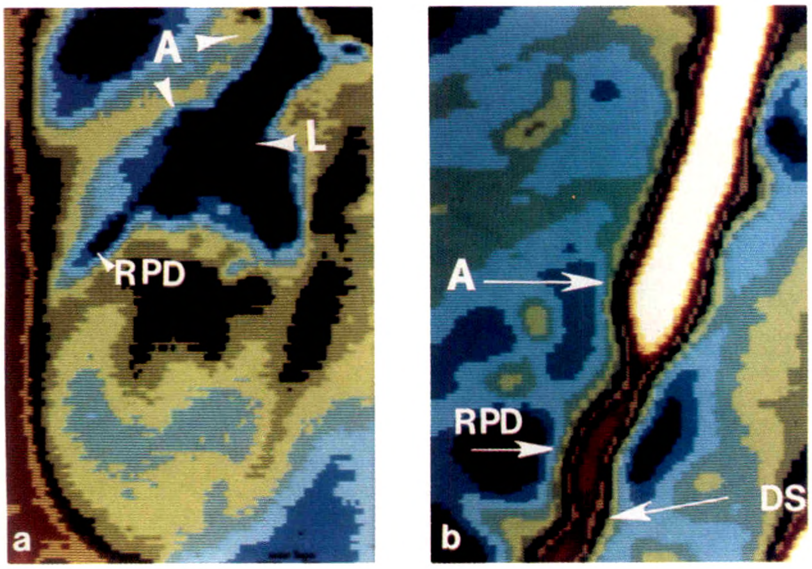

Fig 9. Thermal coronary angiograms of (a) right posterior coronary artery vein graft (RPD) *with anastomotic* (A) *leak* (L) *and (b) the same anastomotic site after leak repair and injection of cardioplegic solution at room temperature, which delineates the diffusely diseased coronary anatomy* (DS).

and the circumflex marginal, 2.1 for the right posterior descending, and 1.9 for the second diagonal bypass grafts. The average for the LAD and proximal right coronary arteries was adversely affected by the increased incidence of pericardial fat around these vessels. For the circumflex marginal and right posterior descending vessels, the problem was positional and due to camera angulation. The reason for the low second diagonal scores was related to the increased incidence of muscle bridges that obscured the vessel.

Comment

Others have previously attempted thermographic imaging of the heart and coronary arteries with less success. The use of infrared thermography for assessing coronary blood flow and bypass graft perfusion was reported in 1971 by Senyk and co-workers [11], who showed in a canine model that epimyocardial temperature decreased after ligation of the LAD. Later, Robicsek, Tzivoni, and associates [5, 12] found that epicardial temperatures correlated directly with the magnitude of reduced coronary blood flow and that the appearance of new cold spots correlated with persisting ischemia. Daniel, Papp, and co-workers [13–15] found that vasodilators increased the temperatures of ischemic regions by improving the collateral flow. More recently, Adachi and colleagues [16] observed that reperfusion after prolonged coronary occlusion (>30 minutes) did not result in return of epimyocardial temperatures to either the preocclusion level or the temperature of adjacent nonoccluded areas.

The application of thermography for evaluating bypass grafts was reported in 1979 by Brydon, Robicsek, and their associates [17, 18]. By injecting saline solution into the proximal end of vein grafts, they were able to recognize epimyocardial perfusion distal to the vein grafts and to roughly delineate the graft and coronary anatomy. Shabbo and Rees [7] correlated thermographic patency with electromagnetic flow measurements; thermographic graft patency correlated with high electromagnetic flow rates. Despite these results, TCA has not been used in routine coronary artery bypass procedures because the equipment has been cumbersome and the actual images were of poor quality [4].

This study describes the application of TCA to real-time assessment of bypass graft patency, details of anastomoses, and native coronary anatomy within the operative field. This technique, as previously reported [6, 13, 16], can also be applied to determine regions of myocardial perfusion during routine coronary artery bypass grafting. Standard surgical technique for bypass grafting in this institution includes injection of supplemental cold cardioplegia into vein grafts and the release of a bulldog clamp on IMA grafts to assess hemostasis. Therefore, the performance of TCA during these surgical maneuvers did not interfere with or delay the conduct of the operation beyond prior placement of the thermal camera. This experience proves both the feasibility and the clinical relevance of TCA.

This report of successful application during routine surgical procedures was made possible by incorporating two major technical advances: use of a new camera system, the AGA 782 or 870, with higher spatial resolution and electronic cooling, and the use of an on-line digital image processor (TIC 8000). Even during the conduct of this study, a technical advance was made and proved to be important: the electronically cooled AGA 870 camera was much easier to handle, allowed full tilting, and made imaging of the posterior and inferior cardiac walls more practical. In addition, evolution of coronary artery bypass grafting technique that routinely employs cold cardioplegia now provides the required critical temperature gradient for thermal vein graft angiography to be done as an integral part of the procedure. As a result, the modern thermal camera system used in this study provided excellent images that did not interrupt but actually augmented the surgical procedure. The image quality obtained proved to have a spatial resolution of 0.1 to 0.2

mm, thereby allowing the detection of smaller side branches. Detection of stenoses was possible starting with estimated 30% lesions, which correlated with experimental laboratory findings comparing TCA with cineangiography of the coronary arteries [19].

Digital image processing further improved the quality of the images, and provided a basis for precise analysis of graft anastomoses and coronary anatomy. We found that of ten different digital image processing techniques, the color mode, image scaling, inverting, magnifying, and low and high pass filtering were the most helpful. The black and white mode allowed immediate orientation and was sufficient for most analyses; the color mode proved to be invaluable in determining the magnitude of stenoses. Scaling provided contrast enhancement; low pass filtering resulted in smoothing of the images; and high pass image filtering enhanced and sharpened the edges. Magnification was particularly helpful in the study of anastomotic and native coronary stenoses. Inversion permitted us to create a uniform image format for warm and cold injectants. This proved to be valuable for rapid orientation during operation and for standardized reading. Image subtraction theoretically could eliminate external influences, such as operating room lights, but we found it was of limited value because of movement during image acquisition.

Although we have refined the optimal variables for intraoperative TCA, it would seem that for it to be of routine clinical usefulness, additional practical developments may be necessary. These include the development of other lenses with zooming and autofocus capability, and camera mounting to the operating room lights. In addition, a more simple image-processing system needs to be developed for image enhancement. Acquisition and storage of data need to be made with a single keystroke for vein and IMA grafts. Ultimately, the ability to generate real-time thermal coronary angiographic image hard copies will permit immediate incorporation into patient records.

Perhaps the two most important results of this study are the ability to immediately document the anatomical integrity of the surgical procedure and the consequent 16% patient incidence in which intraoperative decision making was affected. In addition, we have shown patterns of normal and abnormal flow distribution. Where flow was abnormal, we have demonstrated anastomotic and native coronary artery stenoses to account for these defects. Thermal coronary angiography also detected simultaneous perfusion in more than one vessel, thereby aiding in subtle decisions concerning the need for and location of additional grafts. In diffuse distal coronary disease or anastomotic stenoses where anterograde flows were impaired, TCA gave a much more realistic operative evaluation of the probable outcome and allowed us to determine when nothing further needed to be done to revise the anastomoses. Finally, in IMA grafts where conventional assessments are not definitive, anastomotic sites are clearly depicted by TCA, and both spasm and stenoses in the graft itself are readily detected. The fact is that in complicated situations, in learning situations, and where there is a potentially hostile environment, visualization of the graft anastomoses and the myocardium perfused by the graft has the potential to document the decision-making process and validate the procedure. Thus, although intraoperative verification of bypass graft patency may certainly be thought by some to be unnecessary, the simplicity of the procedure and the unique information it provides suggest to us that it is appropriate to proceed with further evaluation to determine whether it will eventually be worthy of routine clinical use.

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REVIEW OF RECENT BOOKS

Cardiac Arrhythmias: Recent Progress in Investigation and Management

Edited by T. Iwa and G. Fontaine
New York, Elsevier Science Publishing, 1988
385 pp, illustrated

Reviewed by Creighton B. Wright, MD

This volume catalogs the progress made in investigation and management of cardiac arrhythmias in the past two decades by major contributors to this endeavor. It is the result of an international symposium on cardiac arrhythmias participated in by many of the major figures in this area.

The volume is well outlined and readable, while also having extensive depth in terms of the anatomical, electrophysiological, and surgical aspects. It is not a surgical text specifically, although it certainly gives the basis and background for current surgical interventions. The volume has been put together from a meeting in 1986 but still appears to be relevant and very up-to-date, and should serve as an introduction as well as an excellent reference volume for those interested in the fields of electrophysiology and surgical intervention.

This volume certainly will challenge the resident-level reader and is not light reading even for the experienced cardiovascular surgeon and arrhythmia surgeon.

Cincinnati, Ohio

Mediastinal Fibrin Glue: Hemostatic Effect and Tissue Response in Calves

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There is continued controversy regarding the effectiveness and potential adverse effects of fibrin glue. Thus, we chose to evaluate it in a model of experimental calf aortic valve replacement that has been previously well established. Concentrated fibrinogen and topical thrombin were sprayed to form a thin layer of fibrin glue over the mediastinal tissues of 20 consecutive calves undergoing aortic valve replacement. Chest tube outputs of these animals were compared with those of the preceding 20 consecutive calves undergoing aortic valve replacement without fibrin glue. All procedures were performed by the same surgeon, and no other technical changes were made between the two series. Total postoperative chest tube output (mean ± standard error) was 553 ± 50 mL for the calves treated with fibrin glue and 1,155 ± 103 mL for the control calves ($p < 0.001$). On histological examination of mediastinal tissues from 5 treated calves killed 6 weeks after operation, there was no evidence of inflammation, fibrosis, or residual fibrin. To our knowledge, this is the first controlled laboratory study to show that fibrin glue spray is an effective hemostatic agent and that it produces no long-term tissue reaction.

(Ann Thorac Surg 1989;47:450–2)

Fibrin glue is available commercially in Europe as a fibrin sealant system that has been used for several years for surgical hemostasis and tissue adherence during both cardiac and other operations [1–3]. As methods for producing concentrated fibrinogen from single-donor human plasma have been developed, fibrin glue has gained acceptance in the United States [4, 5]. It has been used at a number of medical centers as a hemostatic agent during cardiac operations [6, 7]. At the University of Virginia, it has been used successfully for a wide range of surgical applications since April 1985 [8]. We have also developed a technique for the spray application of fibrin glue using disposable pump-sprayer vials [9]. This technique has resulted in reduced perioperative bleeding for patients undergoing cardiac operations [10]. Nevertheless, to our knowledge, no standardized laboratory proof of the effectiveness of the intraoperative mediastinal spray application of fibrin glue exists. In addition, the potentially damaging effects of mediastinal fibrin glue spray by the production of local inflammation, tissue reaction, and fibrosis have not been determined. This study investigates the effectiveness of the spray application of fibrin glue to the mediastinum of calves undergoing standardized experimental aortic valve replacement, and provides histological analysis of specimens of treated mediastinal tissues.

Material and Methods

Twenty consecutive male calves aged 2 to 3 months and weighing 70 to 80 kg underwent aortic valve replacement through a right thoracotomy. They received simultaneous spray applications of concentrated human fibrinogen [5] and topical bovine thrombin (1,000 NIH units/mL; supplied by Parke-Davis, Morris Plains, NJ) using disposable pump-spray vials [9] to form a thin layer of fibrin glue over all cannulation sites, the aortic suture line, the pericardiotomy, and the intercostal incision. Two 32F Silastic tubes (Dow Corning, Midland, MI) were placed through separate stab wounds in the right chest before closure of the incision to monitor bleeding postoperatively. The calves were given heparin sodium (3 mg/kg) during cardiopulmonary bypass; it was reversed with protamine sulfate after removal of the cannulas.

Postoperatively the calves were allowed to recover from general anesthesia. Chest tube output was measured, and the chest tubes were removed when no further active bleeding was present (four to eight hours postoperatively). Total chest tube output was recorded for each calf. All animals were cared for under a protocol established by the University of Virginia Animal Research Committee.

The results in these 20 calves were compared with those in the preceding 20 calves, in which experimental aortic valve replacement was performed without the application of fibrin glue. Mean values and standard errors for chest tube outputs in the two groups were calculated and compared by unpaired Student's t test. All operations were performed by the same surgeon, and no technical changes were made between the two groups.

Six weeks postoperatively, 5 calves in the fibrin spray group were killed for pathological evaluation of the experimental aortic valve bioprostheses. At the time of death, representative hematoxylin and eosin–stained sections of left ventricular myocardium and ascending aorta were evaluated with light microscopy for evidence of

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Table 1. Chest Tube Output in Calves With and Without Fibrin Glue Spray Treatment[a]

	Operative Group	
Individual values	Control (n = 20)	Spray (n = 20)
1	735	165
2	1,560	300
3	760	265
4	1,225	310
5	950	650
6	950	520
7	2,200	400
8	1,250	1,025
9	1,290	700
10	715	640
11	425	460
12	1,235	475
13	920	575
14	1,375	800
15	1,225	650
16	1,645	435
17	720	475
18	1,300	1,010
19	2,015	550
20	610	660
Mean ± standard error[b]	1,155 ± 103	553 ± 50

[a] Data are shown in milliliters. [b] Significance: $p < 0.001$, control versus spray, by unpaired *t* test.

tissue inflammation, reaction, or residual fibrin. To ensure that the sections were taken through areas that had been sprayed with fibrin glue, care was taken to include the aortotomy suture line.

Results

The mean chest tube output of the calves undergoing aortic valve replacement with the spray application of fibrin glue was compared with the mean chest tube output of the calves undergoing aortic valve replacement without fibrin glue. The results are shown in Table 1. The mean chest tube output (± standard error) of the spray group was 553 ± 50 mL, and the mean chest tube output of the control group was 1,155 ± 103 mL (Fig 1). This difference is significant by unpaired Student's *t* test ($p < 0.001$). The control group of calves is representative of more than 60 calves having operations without fibrin glue. In this larger group, mean chest tube output was 1,466 mL.

There was no gross evidence of tissue reaction. Histological sections from the 5 fibrin glue–treated animals disclosed no residual fibrin, fibrosis, or inflammation 6 weeks after operation. Figure 2 is a photomicrograph of a longitudinal cross section through an aortotomy closure. There is no inflammation or tissue reaction on the adventitial surface or immediately around the artifactual defect left by a suture. Figure 3 is a photomicrograph of a section of left ventricular epicardium sprayed with fibrin glue. There is no inflammation or tissue reaction on the epicardial surface.

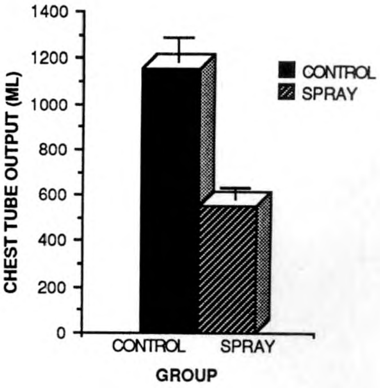

Fig 1. Chest tube output in calves undergoing standardized aortic valve replacement. This is a reduction in output with spray application of fibrin glue. Standard errors are indicated by bars.

Comment

To our knowledge, this is the first published report of a large series of animals showing a significant improvement in hemostasis by the spray application of fibrin glue in a standardized laboratory model. The study demonstrates the effectiveness of spray application of fibrin glue to the mediastinum of calves undergoing standardized experimental aortic valve replacement. There was a highly significant reduction in chest tube output in the calves undergoing valve replacement with spray application of fibrin glue versus the calves undergoing valve replacement without fibrin glue (553 ± 50 mL versus 1,155 ± 103 mL). By having the same surgeon perform the same

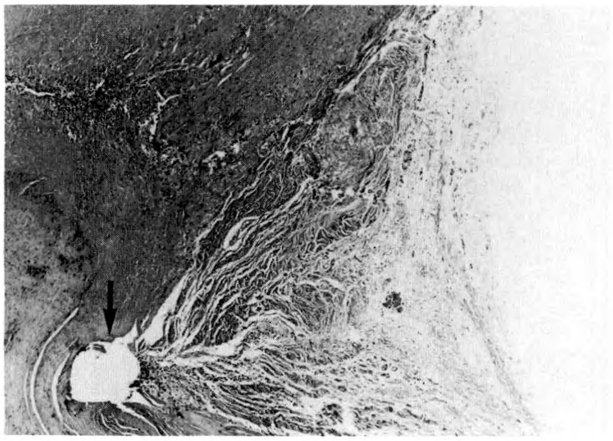

Fig 2. Microscopic section through the aortotomy closure in a calf sprayed intraoperatively with fibrin glue reveals no evidence of inflammatory reaction, fibrosis, or residual fibrin. The arrow denotes the defect produced by suture closure of the aorta. (Magnification, ×50 before 50% reduction.)

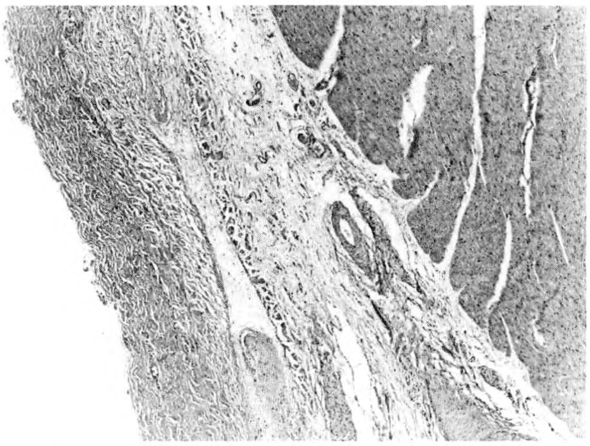

Fig 3. Microscopic section of left ventricular myocardium shows no evidence of residual fibrin glue at the epicardial surface. (Magnification, ×50 before 50% reduction.)

procedure in an animal model, we reduced the interference produced by a large number of uncontrollable variables that affect clinical hemostasis. Thus, the specific hemostatic effect of the spray glue alone has been measured.

Gross and microscopic examination of histological sections from 5 treated calves revealed no inflammatory foreign-body reaction or fibrosis, and no trace of residual fibrin was seen. A lack of fibrosis and a gradual reduction in the amount of residual fibrin over a period of 14 days has been found by others [11] after the use of a European commercial fibrin sealant on pulmonary parenchyma in the rabbit pleural cavity. Fibrin was present within blood vessels in our histological sections, thereby confirming that our fixation, embedding, and sectioning techniques did not remove it.

Our fibrin glue, unlike the European commercial product, does not contain any antifibrinolytic agent, and hence fibrin would be expected to be even more rapidly lysed. Thus, no residual fibrin should be present at the sites of the glue application 6 weeks postoperatively. This tends to confirm that this hemostatic agent produces no long-term adverse local effects. This fact is particularly important in regard to the potential development of constrictive pericarditis. Because fibrin glue does not produce an inflammatory reaction, it is unlikely that it would precipitate a pathological pericardial response.

One criticism of this study could be the use of historical control calves for comparison with those having spray application of fibrin glue. However, the animals were operated on in sequence by the same surgeon, and no known change in technique occurred between the two groups other than the application of glue. In addition, the control group is representative of a larger group of more than 60 calves undergoing experimental aortic valve replacement, within which chest tube outputs have remained similar.

We conclude that fibrin glue is an effective hemostatic agent that produces little local reaction when applied to mediastinal structures during cardiac operations.

We thank Barbara Hoover and Carole Hoadley for their assistance in the preparation of the manuscript.

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Pacing Lead Fracture After a Deceleration Injury

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Acute pacemaker malfunction is potentially lethal. A high index of suspicion must be maintained in physicians caring for traumatized patients utilizing permanent pacing systems. We present a case of transvenous pacemaker lead fracture sustained in a vehicular deceleration injury.

(Ann Thorac Surg 1989;47:453–4)

The debility associated with acute pacemaker malfunction may be immediately fatal, depending upon the nature of the pacemaker malfunction and the ability of the patient's underlying rhythm to sustain life. Injuries causing pacemaker malfunction have accurately been likened to injuries of a vital organ. Prompt recognition and appropriate management must be accomplished if acute pacemaker malfunction develops after trauma. In this report we present a case of transvenous pacemaker lead breakage after deceleration injury in a vehicular accident.

The patient is a 62-year-old man who underwent coronary artery revascularization in 1979 and insertion of a permanent VVI pacemaker in 1980 for sick sinus syndrome. He was seen at Loyola University Medical Center after a deceleration injury incurred while driving his automobile and hitting a large hole in the pavement. Excepting minor injuries, he complained only of light-headedness, and electrocardiogram documented sinus bradycardia at 55 beats per minute without pacing. Magnet application did not elicit an asynchronous, paced rhythm. Pacemaker capture could not be produced by reprogramming to higher pulse width and amplitude. Chest roentgenogram revealed a radiologically intact pacing system 6 weeks before injury (Fig 1), compared with the roentgenogram after injury, which revealed fracture of the transvenous pacing lead (Fig 2).

The patient was taken to the operating room, where the fractured pacing lead was removed and a Medtronic unipolar pacing system was implanted. Postoperatively, he made a complete recovery.

Comment

Large numbers of patients require permanent pacing systems. Approximately 106,000 implantations were performed during 1986 throughout the United States. Acute pacemaker failure can be an immediately life-threatening condition, and the physician must be knowledgeable of all possible causes of acute pacemaker failure.

Acute pacemaker failure may be caused by generator malfunction, lead dislodgement, exit block (endomyocardial fibrosis adjacent to the pacing electrode), lead fracture, or insulation breakage. Literature review with respect to pacemaker malfunction and trauma reveals breakage of permanent pacemaking leads associated with multiple trauma due to a direct blow [1] or physical exertion [2], lead dislodgement after deceleration injuries [3–5], and generator failure due to transistor damage after blunt injury [4].

The electrocardiogram of the patient reported in this case study reveals complete absence of pacemaker function upon presentation, with magnet stimulation, or after reprogramming to higher levels of amplitude and pulse width. Chest roentgenogram confirmed the presence of lead fracture, which was a new finding compared with a recent roentgenogram. Although it is not possible to definitively document the cause of the lead fracture, the deceleration injury appears to have been causative, as the clinical syndrome of acute pacemaker malfunction and the roentgenographic finding of lead fracture were both new findings.

In light of the large number of patients requiring

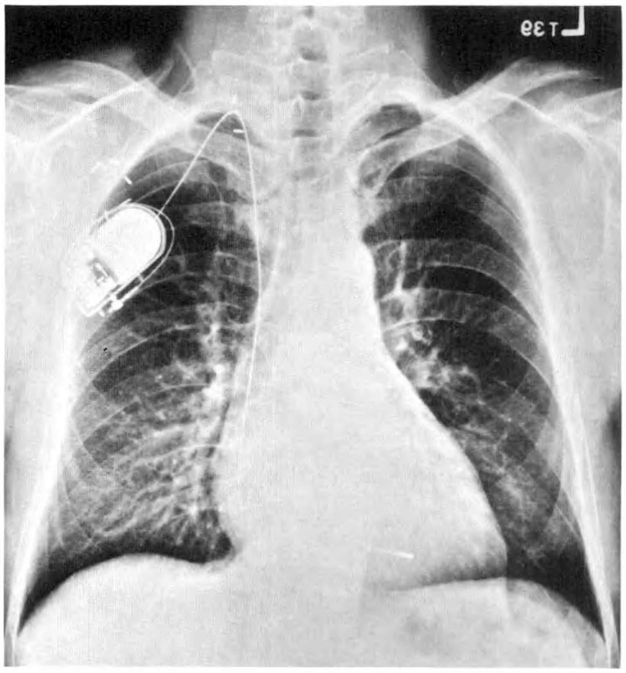

Fig 1. Chest roentgenogram of patient with functioning VVI pacing system.

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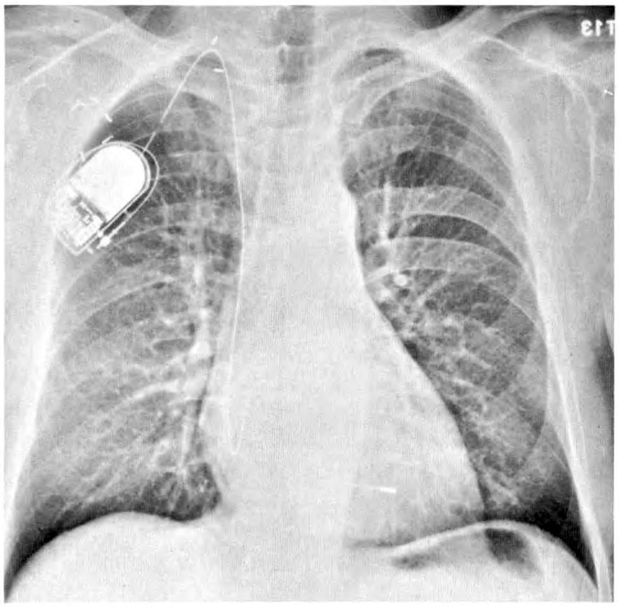

Fig 2. Chest roentgenogram of patient immediately after blunt trauma, revealing fracture of transvenous pacing lead.

pacemaker systems, a constant awareness of the possibility of trauma-related pacemaker malfunction is required in physicians caring for traumatized patients. Acute pacemaker malfunction may require immediate reprogramming of the generator or insertion of a temporary pacing system, or both, before operative correction. For those patients who are pacemaker-dependent, the pacing system is indeed a vital organ.

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Entrapment of Broken Guidewire in the Left Main Coronary Artery During Percutaneous Transluminal Coronary Angioplasty

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The distal end of a flexible, steerable guidewire broke during an attempted percutaneous transluminal coronary angioplasty of the left anterior descending coronary artery and was retained in the left main coronary artery. It was successfully removed surgically. Etiology of, management of, and precautions for avoiding this complication are discussed.

(Ann Thorac Surg 1989;47:455–7)

Percutaneous transluminal coronary angioplasty (PTCA) is an accepted and proven mode of therapy in selected patients with coronary artery disease. The reported success rate is over 90%, but approximately 3% to 7% of patients may require an urgent operation to treat acute myocardial ischemia either due to acute occlusion, perforation, or dissection of the coronary artery or due to a thromboembolic event during attempted angioplasty [1–3].

The complications associated with guidewires, which are used during angioplasty, are rare and often unrecognized. We report a case in which the distal end of a USCI flexible, steerable guidewire (C.R. Bard, Inc, Billerica, MA) broke during the PTCA and was retained in the left main coronary artery, requiring urgent surgical intervention for its retrieval.

The patient, a 68-year-old man, was first evaluated in Asheville Veterans Administration Medical Center in April 1987 for progressively increasing angina pectoris. An exercise treadmill test was positive in stage II. Coronary arteriogram revealed 90% stenosis of the left anterior descending coronary artery. The patient underwent successful PTCA with complete relief of symptoms. Four months after angioplasty exertional angina redeveloped. The treadmill test was positive at eight minutes, which was unchanged from the postangioplasty evaluation. Coronary arteriogram showed recurrence of substantial stenosis at the site of previous dilatation. A repeat angioplasty was recommended. After administration of 10,000 units of heparin, a left coronary guiding catheter was passed into the ostium of the left coronary artery and a 2.5-mm ACS balloon catheter (Advanced Cardiac Systems, Mountain View, CA) was passed over a 0.014-inch USCI Steerable Veriflex guidewire to the end of the guiding catheter. Multiple attempts to pass the guidewire through the stenosed segment of the left anterior descending coronary artery were unsuccessful, and it had a tendency to fall into a smaller diagonal branch. During one of these attempts, the end of the floppy guidewire broke off and became wedged in the left main coronary artery. The free portion of the wire extended freely into the lumen of the ascending aorta (Fig 1). The remaining portion of the guidewire, the balloon dilating catheter, and the guiding catheter were removed. During the procedure, the patient had no angina or hemodynamic instability. To prevent thrombus formation with possible occlusion of the left main coronary artery or embolization of the broken guidewire to other organs, and because the patient needed a revascularization procedure, we elected to proceed with operation. No attempts were made to extract the wire using catheter techniques. The left internal mammary artery pedicle was dissected off the chest wall. The patient was cooled to 20°C soon after initiation of cardiopulmonary bypass. The heart was fibrillated and the aorta was cross-clamped. A small aortotomy was made. The guidewire was seen to be firmly lodged in the left main coronary artery. It was extracted without difficulty. There was no obvious damage to the coronary artery or to the aorta. The aortotomy was repaired and cold cardioplegic solution was infused. The left internal mammary artery pedicle was anastomosed to the left anterior descending coronary artery. The patient was weaned off the cardiopulmonary bypass without difficulty. The postoperative course was uneventful and the patient continues to be asymptomatic at 5 months of follow-up.

Direct inspection of the removed segment of the guidewire revealed it to be intact in the distal 3 mm; proximal to this point the single platinum coil had become unraveled (Fig 2).

Comment

Percutaneous transluminal coronary angioplasty has gained wide acceptance as a therapeutic option in the treatment of coronary artery disease in many patients and

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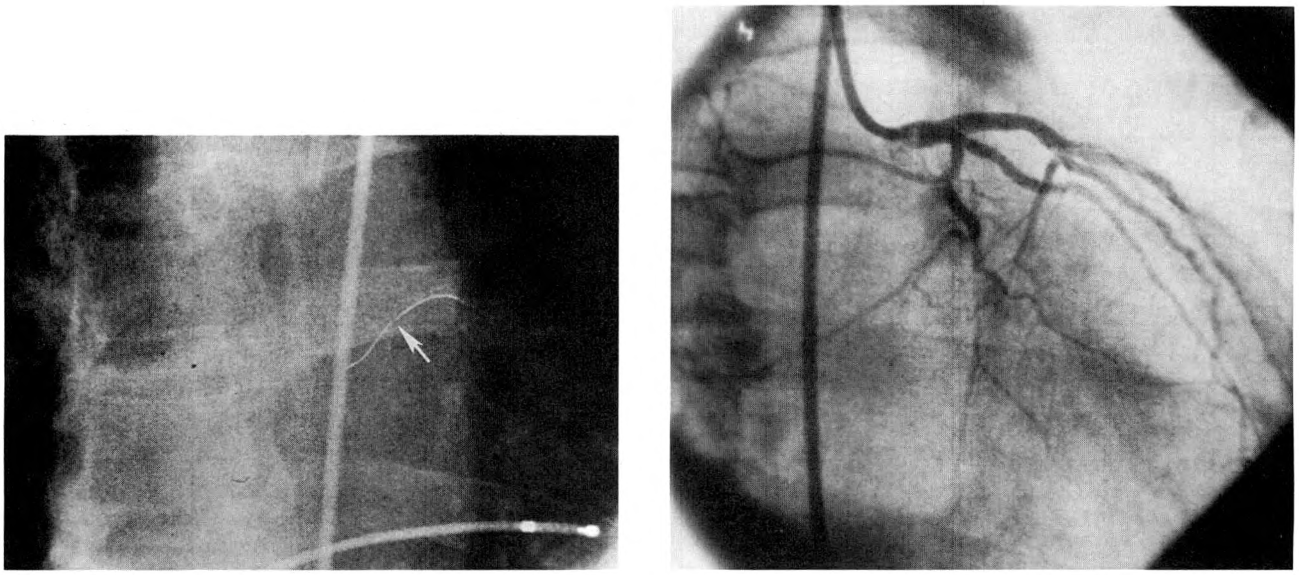

A B

Fig 1. A. Left anterior oblique view, showing retained guidewire in the left main coronary artery. The distal end of the wire is free in the ascending aorta. The translucent area in the distal part of the guidewire (arrow) *suggests overstretched coils. The unraveled single platinum coil is not seen on this film. B. A left coronary arteriogram in a similar view demonstrating the coronary anatomy.*

is being safely performed repeatedly in most of the cardiac catheterization laboratories of this country. With the introduction of the flexible, steerable guidewire, the primary success rate has greatly improved while the incidence of serious intraoperative complications has markedly decreased. However, occasionally the guidewire itself may cause serious complications such as perforation or dissection of the distal coronary artery. Recently, uncoiling and fracture of the distal end of the guidewire has been reported [4–7]. The precise incidence of this complication is not known. Hartzler and associates [7] reported eight instances of fracture and retention of guidewire fragments within the coronary circulation that were experienced in 5,400 consecutive PTCA procedures. The fracture of the guidewire may be caused by a number of mechanisms. Usually, the guidewire is advanced for a considerable distance beyond the stenotic lesion so that the balloon catheter can be guided easily across the lesion. If the guidewire is advanced too far in a small branch of the coronary artery, there is a possibility of wedging the wire. Once wedged, traction on the wire may cause unraveling of the platinum coil, thus weakening it. Further traction may result in fracture of the wire. It is also possible for the guidewire to get wedged between the guiding catheter and the coronary artery. Overrotation of the wire beyond 180 degrees in either direction, especially if the tip is not free, may also cause unraveling of the platinum coil and fracture of the wire.

Platelets and fibrin may deposit over the retained guidewire, which may result in thrombotic occlusion of the coronary artery. In our patient, this could have been a life-threatening situation as the guidewire was entrapped in the left main coronary artery. The fibrin and platelet deposits from the segment of wire protruding in the ascending aorta may embolize to cerebral and other peripheral vessels. The risk of embolization of the wire itself

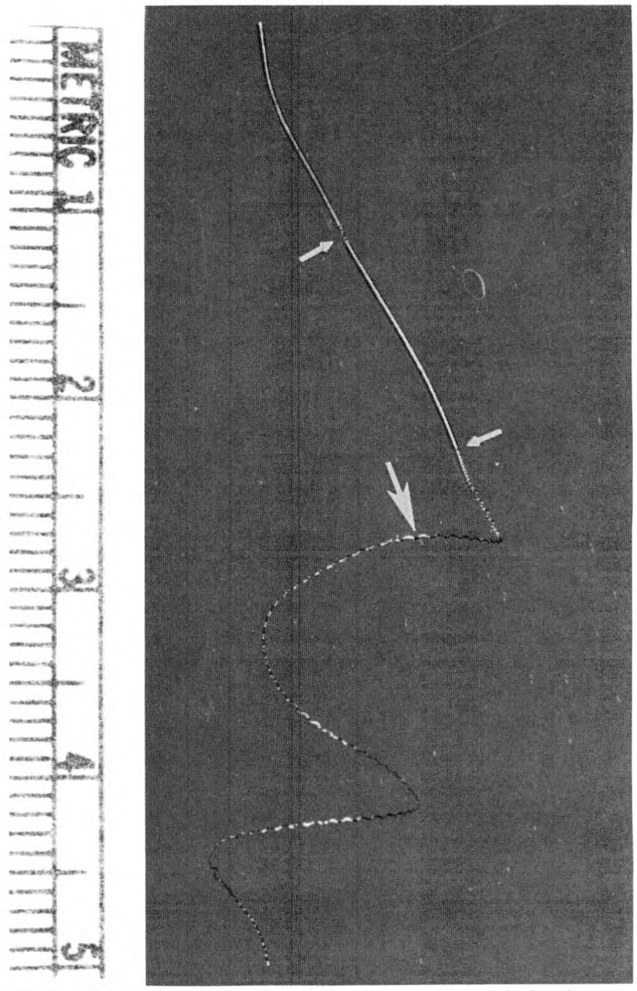

Fig 2. The extracted guidewire shows sites of overstretched coils (small arrows). *The single platinum coil had unraveled* (large arrow). *This is not seen on the cineangiography film.*

is low because usually it is firmly fixed within the coronary artery.

Retained intraarterial foreign bodies can be retrieved by several nonsurgical techniques. Steele and co-workers [6] successfully retrieved an intraaortic segment of guidewire fragment by using a Dotter retrieval catheter. Hartzler and associates [7] used pigtail and Amplatz catheters as well as bioptomes to retrieve fractured wires. However, one must be careful in using these techniques because occasionally the wire may become free and embolize to the cerebral or peripheral circulation. Small fragments of wire may be left within the coronary artery without adverse sequelae, especially if they are contained within chronically occluded vessels [7].

We elected to proceed with operation in our patient because the guidewire was lodged in the left main coronary artery and the patient needed a myocardial revascularization procedure for relief of ischemic symptoms. The wisdom of using the internal mammary artery instead of a vein graft in this situation may be questioned as the vein graft procedure would have taken less operative time. However, because the patient was hemodynamically stable and had no ischemic electrocardiographic changes, we felt comfortable in spending a few extra minutes to take down the internal mammary artery. The internal mammary artery graft should remain patent for an extended period of time in this patient with single-vessel disease.

Several precautions should be taken to avoid this complication during PTCA. Diminished or absent steerability of the guidewire may suggest its entrapment within the coronary artery. If this occurs, then the wire should be gently withdrawn. If this maneuver fails and the wire begins to uncoil (as evidenced by the appearance of a segment of radiolucency in the guidewire), then the guiding catheter should be advanced in the coronary artery to strengthen the fulcrum, and the guiding catheter and the guidewire should be withdrawn together. Finally, overrotation of the flexible steering guidewire should be avoided, especially if its tip is entrapped in the coronary circulation.

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Left Subclavian Arterioesophageal Fistula Induced by a Foreign Body

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A left subclavian arterioesophageal fistula was diagnosed in a 35-year-old man at exploratory thoracotomy for suspected aortoesophageal fistula. After successful closure of the arterial fistula the patient developed a mediastinal abscess and esophagopleural fistula. The latter was successfully managed by retrosternal jejunal esophagoplasty followed by excision of the thoracic esophagus. This report documents a case of left subclavian arterioesophageal fistula and illustrates the importance of early diagnosis and surgical intervention of arterial perforation secondary to a foreign body in the esophagus.

(Ann Thorac Surg 1989;47:458–60)

When a major artery is eroded as a result of a foreign body in the esophagus, an arterioesophageal fistula results and exsanguinating hemorrhage ensues [1–8]. Although the clinical course of this entity is characteristic and well documented in the literature since a description by Chiari in 1914 [3], in the majority of cases the correct diagnosis is not established until after the death of the patient. In the past, the attention of many reports has been centered chiefly on the aortoesophageal fistula and its pathological features. This article describes an unusual fistula between the left subclavian artery and esophagus diagnosed at exploratory thoracotomy for suspected aortoesophageal fistula. To our knowledge, left subclavian arterioesophageal fistula induced by a foreign body has not been previously reported in the English-language literature.

The patient, a 35-year-old man, was first admitted to a general hospital because of retrosternal discomfort on swallowing and deep breathing after ingesting a piece of goose bone three days earlier. Both roentgenographic and esophagoscopic examinations revealed no foreign body. Only a small abrasion was seen on the left lateral wall of the esophagus 20 cm from the incisor. The patient was sent home after the esophagoscopy. He remained well until four days later (1 week after he swallowed the goose bone), when he collapsed in the street after an attack of retrosternal pain and a bout of hematemesis. After readmission to the general hospital, he vomited 1 L of fresh blood. Emergency upper endoscopy was performed, which disclosed an ulcer overlying a hematoma on the left lateral wall of the esophagus, 20 cm from the incisor. The rest of the esophagus, the stomach, and the first part of the duodenum were normal. A Sengstaken-Blakemore tube was inserted and the esophageal balloon was inflated. The patient was transferred to us after transfusion of 2 units of blood.

On admission to Grantham Hospital, the patient did not have any abnormal physical signs except for a body temperature of 38.3°C. His hemoglobin was 11.1 g/dL and his white blood cell count was 28 × 10^9/L. His chest roentgenogram showed an in situ Sengstaken-Blakemore tube, widening of the superior mediastinum on the left side, and streaks of gas in the mediastinum. Aortoesophageal fistula was suspected and emergency exploratory left thoracotomy was performed.

At operation, the left pleural cavity was found to contain 30 mL of slightly turbid fluid; the apex of the left lung was adherent to the mediastinum. The left lung itself was normal. The left subclavian artery was encased in an inflammatory mass, 4 × 3 × 2 cm. This mass was composed of blood clots and foul smelling necrotic tissue. A 1-mm perforation was found on the posteromedial wall of the left subclavian artery 2 cm from its origin (Fig 1). Neither a fistulous opening on the esophagus nor a foreign body could be found. The inflammatory mass, together with a segment of the involved left subclavian artery, was excised and the stumps of the left subclavian artery were closed with running Prolene suture. It was thought that the esophageal opening had sealed off. The pleural cavity was rinsed with 0.25% neomycin solution and the thoracotomy was closed with a large tubal drain positioned in the vicinity of the infected area.

The abscess wall on culture yielded a mixed growth of aerobes and anaerobes. A course of appropriate antibiotics was started. A Gastrografin (E.R. Squibb & Sons, Princeton, NJ) swallow was performed two days later. There was no leakage of the contrast material and nasogastric feeding was started. The patient became afebrile by the fourth postoperative day. However, on the ninth postoperative day, he again ran a temperature with marked leukocytosis. His chest roentgenogram was suggestive of a mediastinal abscess. He was again explored through the previous left thoracotomy.

At reoperation, a 2 × 1-cm perforation was found on the proximal thoracic esophagus above the aortic arch and there was a small collection of foul smelling pus in the vicinity. In view of the large esophageal defect and the

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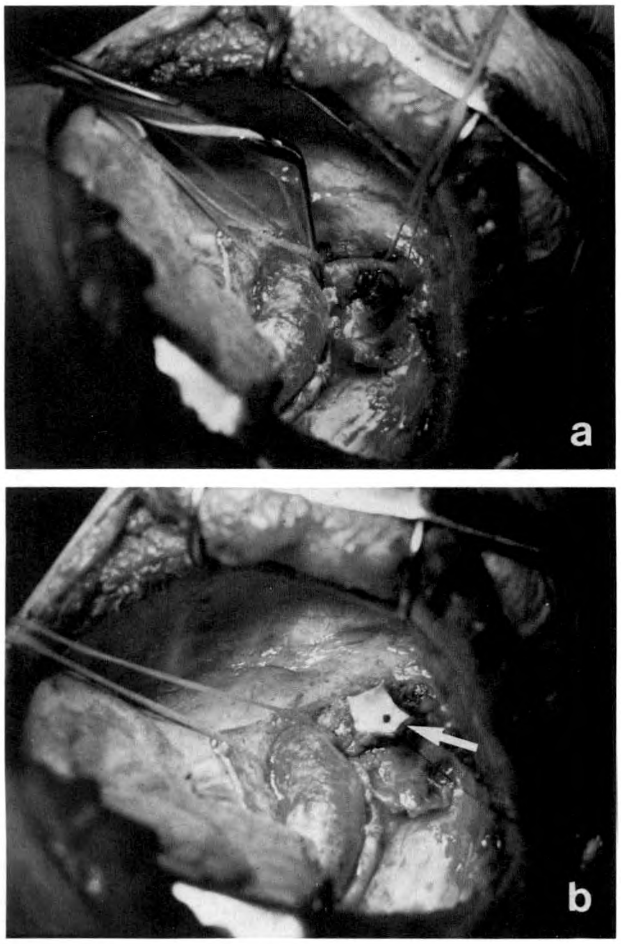

Fig 1. (a) The left subclavian artery being clamped at its origin with encircling tapes around the aortic arch and distal left subclavian artery. There was an inflammatory mass medial and posterior to the left subclavian artery. (b) The left subclavian artery was divided at its origin and 1 cm proximal to its branches. Both the proximal and distal arterial stumps were closed by direct suturing. The excluded segment of artery was laid open in situ to illustrate the site of the fistulous opening (white arrow).

presence of acute infection, no attempt was made to close the defect on the esophagus. The diseased segment of the esophagus was excluded by a terminal cervical esophagostomy and the distal stump was closed. A Witzel gastrostomy was performed for feeding purposes. Culture of the pus in the mediastinum yielded *Bacteroides melaninogenicus*. Eight weeks after the second thoracotomy, his upper gastrointestinal tract was reconstructed with a retrosternal jejunal esophagoplasty. A segment of jejunum was chosen as the conduit because we preferred to retain the stomach as a reservoir and the colon was found to be inadequately prepared. To avoid difficult dissection in the mediastinum after mediastinitis, the retrosternal route was utilized, and for the same reason the remains of the thoracic esophagus were left behind. The latter was excised 1 year later because of recurrent chest wall abscess and persistent cutaneous–esophageal fistula. The patient remained well, and there was no symptom suggestive of subclavian steal syndrome.

Histopathological examination of the excised inflammatory mass and the segment of left subclavian artery showed that the subclavian artery was grossly normal. The fistulous tract at the artery led directly to an area filled with necrotic materials and abundant microorganisms consistent with oral flora. The necrotic materials were compatible with food particles. The area was surrounded on both sides by adipose tissues showing acute suppurative inflammation with abundant granulation tissues.

Comment

The blood vessel most commonly perforated by a foreign body in the esophagus is the aorta 1 to 5 cm from the origin of the left subclavian artery [4]. This is the level of relative narrowing of the esophagus, where foreign bodies are more likely to impact, and is also the level of closest approximation of the aorta and esophagus. Less commonly, perforation occurs at the proximal aortic arch and the lower thoracic aorta or at other intrathoracic vessels. The latter include the intercostal artery and aberrant right subclavian artery [6–8]. To our knowledge, perforation of the left subclavian artery has not been reported in the English-language literature, although it is in close proximity with the upper thoracic esophagus.

The signs of an arterioesophageal fistula are characteristic and well described in the literature. If a clinician is well informed, early diagnosis is extremely easy. The interval between the signal hemorrhage and death from exsanguination is sufficiently long to allow operative intervention. Since the report of this catastrophic lesion by the French naval surgeon Dubreuil in 1818 [1], most clinicians shared Poulet's view that arterioesophageal fistula is "beyond the resources of the healing art" [2]. However, one of us has shown previously [5], and it is also seen in the present case, that prompt surgical intervention can alter this pessimism and change the clinical course of this potentially lethal entity. We would like to propose the following. (1) All patients suspected to have a foreign body in the esophagus should undergo esophagoscopy. (2) When the esophagus has been injured, the patient should be fasted and given tube or parenteral feeding for a few days. A course of appropriate prophylactic antibiotics should also be given. (3) On discharge, patients should be informed of the clinical features of arterioesophageal fistula and instructed to seek medical care immediately when signal hemorrhage occurs. (4) Patients with suspected arterioesophageal fistula should be explored through a left thoracotomy without delay. A left thoracotomy is the best approach because it gives the best access to the site of the fistula. Theoretically, in the presence of exsanguinating hemorrhage, institution of femorofemoral partial cardiopulmonary bypass before thoracotomy would be life-saving. The arterioesophageal communication can be identified without difficulty. It is important that both openings of the fistula are properly repaired. Failure to do so may lead to further operation. As illustrated by the present case, the three major surgical procedures following the initial thoracotomy might have been avoided if a more thorough search had been made for the esophageal perforation at the original thoracotomy and the perforation had been formally repaired. The potentially infected fistulous tract should be excised, including the bleeding artery or part of the arterial wall in the case of the aorta. We believe that direct closure of the arterial defect away from the esophageal opening is preferred and synthetic vascular grafts should be avoided whenever possible.

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Familial Multiple-Organ Arterial Ectasia With Massive Hemoptysis

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Numerous large, thin-walled ectatic arteries up to 1 cm in diameter were encountered during operation on a 20-year-old patient. These vessels covered most of the right pleural surface. Similar symptomatic ectatic vessels were found arising from the left side and intracranially. Eight years later large arteriovenous malformations developed from chest wall and scar tissues that required ligations to control hemoptysis. This case was unique in that extensive multiorgan capillary and arterial systems were involved.

(Ann Thorac Surg 1989;47:461–3)

Arteriovenous (AV) malformations are rare anatomical abnormalities. Cerebral arterial ectasia is an unusual condition that occurs in less than 0.05% of the population [1]. Multiple-organ arterial ectasia is even more rare, and has been scarcely reported in the English-language literature. The well-known Rendu-Osler-Weber syndrome is described as hereditary telangiectasia of the face and gastrointestinal mucosa with hemorrhagic involvement at the capillary level [2]. This report discusses arterial ectasia of the right pleural cavity, right lung, left lung, brain, and chest wall.

A 20-year-old man with massive hemoptysis presented himself to a neighboring hospital in 1978. He had a history of four previous episodes of hemoptysis of unknown origin. A bronchoscopy showed that the bleeding appeared to be from the right upper lobe bronchus. Due to continued massive hemoptysis, the patient was transferred to our institution.

After his arrival at the intensive care unit, the hemoptysis worsened, and he lost approximately 3,000 mL of blood. A bronchoscopy, thoracotomy, and upper lobe lobectomy were performed on the right side. These procedures were complicated by cardiac arrest during anesthesia induction. Cardiac resuscitation, multiple rigid bronchoscopic procedures, and fiberoptic bronchoscopy were required to maintain an open airway. The bleeding was finally controlled using a Carlen's endotracheal tube to completely occlude the right bronchus. The operation required 9.5 hours and was extremely tedious and difficult due to extensive large, thin-walled ectatic AV communications, up to 1 cm in diameter without muscularis. All of these vessels were ligated and divided at their origins from the innominate, internal mammary, subclavian, and bronchial arteries, as well as from numerous vessels coming directly from the descending aorta. The lobectomy could then be performed in the usual fashion. The blood clots that remained inside the right bronchus were removed via the upper lobe bronchial stump. The patient recovered uneventfully.

The pathology report indicated that the lung was hemorrhagic, purplish, and consolidated. The tracheobronchial tree was filled with clotted blood. Multiple dilated, tortuous, and thickened blood vessels were noted; some segments showed aneurysmal dilation and occlusion by blood clots. The microscopic examination revealed large vascular channels showing deficiencies and excesses of muscle components, focal calcification, and thrombus formation. Adjacent alveoli were engorged or hemorrhagic with infarction in some sections, and multiple blood-filled bronchi were seen.

One year later, the patient experienced recurrent hemoptysis, and this time the arteriogram revealed ectatic arteries arising from the left side of the descending aorta travelling into the left lung. These vessels were ligated at their origins to control bleeding. Five years later, the patient developed symptomatic cerebral arterial ectasia, similar to that found in the thorax. The patient later had the aortic valve and ascending aorta replaced at the Texas Heart Institute because of aneurysmal dilations with Marfan's syndrome.

In May 1986, the patient again developed continuous hemoptysis. An arteriogram showed marked enlargement and tortuosity of the lateral thoracic artery, the thoracic branch of the thoracoacromial artery, the highest thoracic artery, and the internal mammary artery of the right thorax (Fig 1). Extensive collateral circulation was seen along the entire chest wall.

The intercostal arteries (T-5 to T-9) coming from the descending aorta were also dilated. All, as well as the chest wall arteries, apparently supplied a large AV malformation within the chest wall (Fig 2). It is likely that the malformation involved at least part of the right pulmonary vessels and therefore traversed the pleura. There was a large blush in the delay film that had the appearance of a markedly increased number of enlarged vessels. This could have been vessels within the lung parenchyma that developed from scar tissues between the visceral and parietal pleura. Multiple ligations of these vessels near their origins within the chest wall successfully controlled

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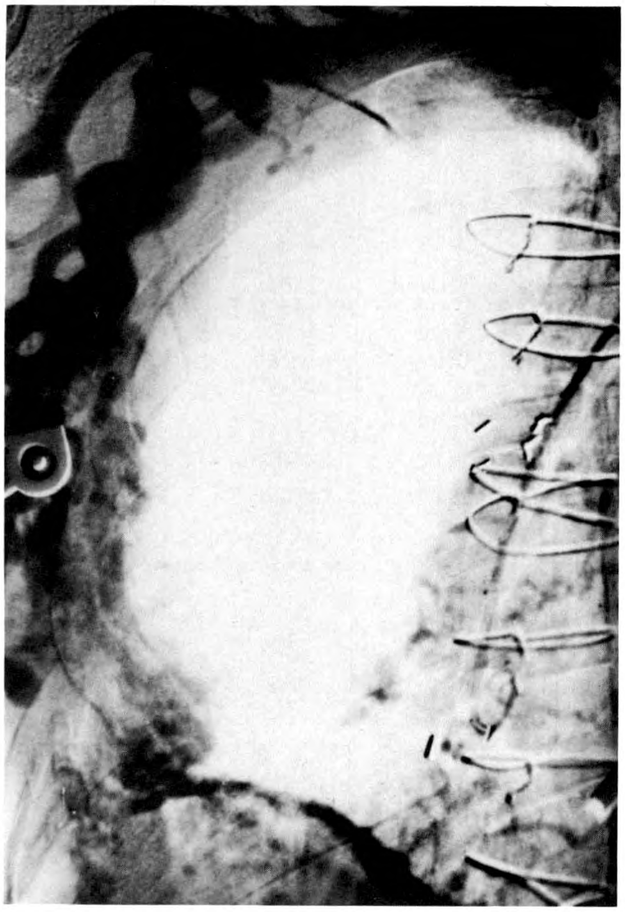

Fig 1. Ectasia of the thoracic branches of the right subclavian artery.

the hemoptysis. The patient has done well so far with continued anticoagulation, and has had no further hemoptysis.

Comment

Congenital AV aneurysms, megadolichoarteria, and serpentine arteries are among the many terms used to describe the condition of arterial ectasia [3–6]. Examination of some of these pathological vessels showed patchy sclerosis of the intima, gross thickening of the arterial wall, and hyaline degeneration of the muscular layers [1, 4, 7]. More importantly, it seems that the loss of the elastic membranes is consistently documented [1, 4, 7]. Progression of the arterial ectasia appears to depend on the association of hypertension, arteriosclerosis, and loss of arterial elastic membrane [8]. The pathological findings of this patient revealed large vascular channels showing deficiencies and excesses of muscular components, focal calcification, and thrombus formation.

This case differs from the typical Marfan's syndrome in that it also involves medium and small arteries and capillaries, but does not involve the mitral valve, subluxation of the lens, or cystic medial necrosis of the artery. This patient's case is unique in that extensive multiple-organ arterial and capillary systems and the thoracic artery and its branches were involved in the AV malformations. It includes the ascending aorta, aortic arch, descending aorta, innominate artery, subclavian artery and its branches, internal mammary artery, bronchial artery, intercostal arteries, and arterioli and capillaries of the thorax, as well as cerebral arteries within the brain. Bleeding was excessive during all the operations due to ectatic changes of the intermediate and smaller vessels. The multiple recurrent episodes of this patient predict more problems in the future, and preservation of lung tissue is essential. Selective embolization was not done because of fear of systemic emboli, as the arteriogram showed enlarged sinuses from the scar tissue communicating between the chest wall and right lung.

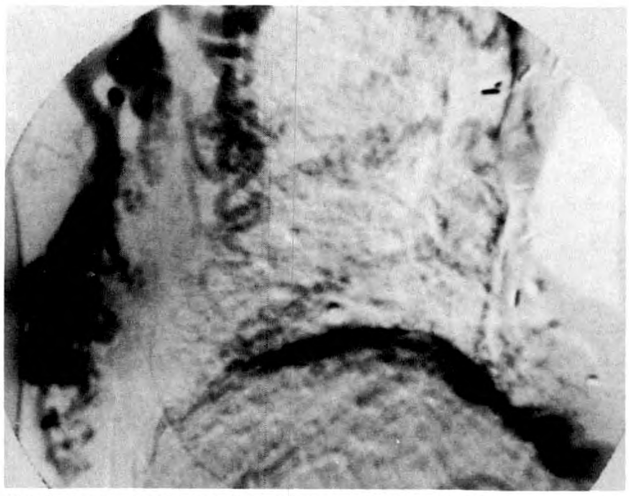

Fig 2. Large ectatic vessels developed within the chest wall and right diaphragm.

Selective embolizations for AV malformations using autologous tissue-absorbable hemostatics, synthetic particulates, liquid polymers, balloons, or coils have been reported [9]. Retrospectively, under well-planned, elective conditions, balloon or coil embolization could have been used as an alternative to surgical ligation, provided that the embolic devices could stay in place in the target area.

The patient's family history includes his brother's similar AV malformations, his sister's AV malformation in the left chest wall, and his grandfather's sudden death from a rupture of "arteries in the chest," with possibly similar conditions. His brother experienced episodes of hemoptysis in 1977. In 1978 several ectatic bronchial arteries were successfully ligated for recurrent hemoptysis. This shows an extremely strong and rare hereditary tendency [10].

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BOOKS RECEIVED

Cardiomyopathies: Clinical Presentation, Differential Diagnosis, and Management. Cardiovascular Clinics, First Edition
Edited by James A. Shaver
Philadelphia: F.A. Davis, 1988
288 pages, illustrated, $75.00

This is a multiauthored book covering all aspects of cardiomyopathy including selection of patients and results of cardiac transplantation.

Trauma, Sepsis, and Shock. The Physiological Basis of Therapy
Edited by George H. A. Clowes, Jr
New York, Marcel Dekker, 1988
587 pages, illustrated

This book is edited by one of the leaders in studies of the physiology of septic shock. He has recruited the leaders in American surgery as his authors. This book should be an excellent reference for the current thinking on sepsis in surgery.

Clinics in Chest Medicine, Vol 9, Number 3, Sep 1988. Pulmonary Effects of AIDS
Edited by Dorothy A. White and Diane E. Stover
Philadelphia: W.B. Saunders, 1988
Illustrated

This short, multiauthored book with authors from the Center for Disease Control, San Francisco, New York, and Bethesda should provide a good source for reference.

Inherited Diseases of the Lung
By Jack Lieberman
Philadelphia: W.B. Saunders, 1988
187 pages, illustrated, $39.95

This is a short monograph on inherited lung diseases. The author points out that inherited lung disease can have its first manifestations in adults. The book may provide a useful reference.

Cardiology 1988
Edited by William C. Roberts
Washington: Butterworth, 1988
505 pages, illustrated, $60.00

The yearly update on advances in cardiology.

Systemic-to-Pulmonary Artery Shunt Using the Internal Mammary Artery

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Systemic-to-pulmonary artery shunts may be useful for palliation of cyanotic congenital heart disease. We report the case of a 5-year-old boy in whom the internal mammary artery was used to create a systemic-to-pulmonary artery shunt after failure of a previous Blalock-Taussig shunt. This technique may have distinct advantages in selected cases and should be considered as an alternative during investigation of the older child who requires a systemic-to-pulmonary artery shunt.

(Ann Thorac Surg 1989;47:464–5)

Systemic-to-pulmonary artery shunts provide palliation of many cyanotic congenital heart lesions in infancy and childhood. A number of shunts have been described since Blalock and Taussig's subclavian artery-to-pulmonary artery anastomosis in 1945 [1]. Present options include the natural or modified Blalock-Taussig shunt, the ascending aorta-to-right pulmonary artery shunt (Waterston), the descending aorta-to-left pulmonary artery shunt (Potts), or the central aorta-to-pulmonary artery graft (Goretex). This report describes the use of the internal mammary artery as a systemic-to-pulmonary artery shunt for repeat palliation in a 5-year-old child with pulmonary atresia, ventricular septal defect, and hypoplastic pulmonary arteries.

A male newborn was initially seen with cyanosis. Cardiac catheterization revealed pulmonary atresia, ventricular septal defect, hypoplastic pulmonary arteries, and a right-sided aortic arch. A left modified Blalock-Taussig shunt was performed using 4-mm polytetrafluoroethylene tubing (Gore-Tex, W.L. Gore & Associates, Elkton, MD) at 3 weeks of age. The patient did well postoperatively, except for mild growth retardation. He was evaluated at 5 years of age because of progressive cyanosis and decreased exercise tolerance. Physical examination revealed a small, cooperative child in no distress. His pulse was 90 beats/min and regular, his respiratory rate was 28/min, and his blood pressure was 100/75 mm Hg in the right arm. His chest was clear and his cardiovascular examination was significant for clubbing and moderate cyanosis of all four extremities. Left arm pulses were absent. All other pulses were normal without a radial-femoral delay. A prominent left ventricular precardial impulse was present and auscultation noted S_1 to be loud with a single S_2 and no ejection click. A 2/6 continuous murmur was heard at the left sternal border with radiation to the back. Abdominal examination revealed no organomegaly. His electrocardiogram demonstrated right ventricular hypertrophy.

On cardiac catheterization, the right atrial saturation was 75%. Cineangiography showed pulmonary atresia and a ventricular septal defect. There was no forward flow into the main pulmonary artery; right and left pulmonary arteries filled later via bronchial collaterals and via the Blalock-Taussig shunt, which was severely stenotic at the pulmonary artery anastomosis. The pulmonary arteries still measured less than 4 mm in diameter with a pulmonary artery-to-aortic ratio of approximately 0.3. Also noted were large bilateral internal mammary arteries without evidence of a coarctation. It was believed that the pulmonary arteries remained too small for total correction by a Rastelli procedure.

During exploration through a right posterolateral thoracotomy, the large internal mammary artery was noted to be 5 mm in diameter, which was measurably larger than the distal right subclavian artery. The internal mammary artery was mobilized from the thoracic inlet to the diaphragm using a technique similar to that used in preparation of the internal mammary artery for myocardial revascularization. All side branches were carefully ligated. An end-to-side anastomosis of the right internal mammary artery to the right main pulmonary artery was performed with interrupted 7-0 Prolene sutures (Fig 1). The internal mammary artery pedicle was sufficiently long to allow a tension-free anastomosis without kinking. With reinstitution of flow, an excellent thrill was palpated and a flow of 150 mL/min through the internal mammary artery was measured by an electromagnetic flow transducer.

The child recovered well and was discharged home four days postoperatively. Follow-up at 6 months revealed increased exercise tolerance without cyanosis.

Comment

Systemic-to-pulmonary artery shunts increase pulmonary blood flow and symptomatically palliate children with complex cyanotic heart disease who cannot be corrected in early infancy [1]. Kirklin, Gale, Alfieri, and colleagues [2–4] have reported growth of the pulmonary arteries after shunting, making later total correction possible. Pulmo-

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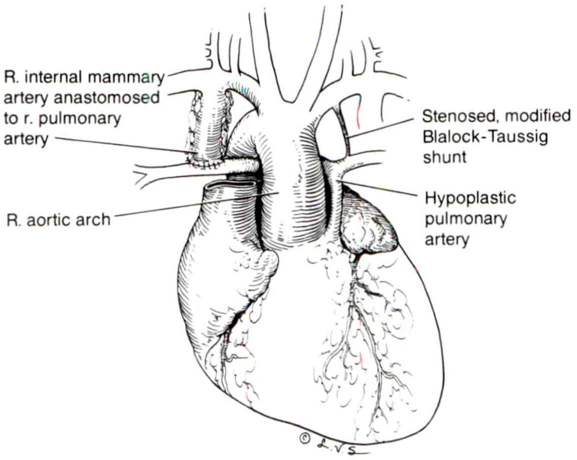
R. internal mammary artery anastomosed to r. pulmonary artery
R. aortic arch
Stenosed, modified Blalock-Taussig shunt
Hypoplastic pulmonary artery
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Fig 1. Anatomy of the right internal mammary artery–pulmonary artery anastomosis.

nary artery enlargement is usually greater than that which occurs due to growth of the child as a whole [3]. Angiographically, the size of both pulmonary arteries can double within 2 weeks of a successful shunt due to increased pulmonary blood flow and pressure [5].

Numerous technical and physiological problems have been described with shunts. Blalock and others have described arterial kinking in constructing the natural subclavian-to-pulmonary artery anastomosis, even if the shunt is performed on the side opposite the aortic arch [6–9]. This procedure also decreases blood flow to the arm, infrequently leading to growth retardation of the involved extremity. Many shunts may cause excessive pulmonary blood flow leading to early pulmonary hypertension. The Potts and Waterston shunts may significantly distort the pulmonary arteries, complicating later definitive repair or takedown of the anastomosis. Finally, prosthetic conduits do not grow with the child, and therefore have limited longevity.

The use of the internal mammary artery for a systemic-to-pulmonary artery shunt was described by Cobanoghe and co-workers [10] as treatment for a child with congenital absence of the right pulmonary artery, congestive heart failure, pulmonary hypertension, and respiratory insufficiency. The anatomy of the internal mammary artery is more suitable than that of the subclavian artery for a tension-free anastomosis to the pulmonary artery without kinking, if it is large enough to provide adequate pulmonary blood flow. The internal mammary artery is more pliable than the prosthetic grafts, offers the advantage of growth and flow adaption, eliminates the risk of prosthetic graft infection, and does not affect blood flow to the arm [11].

It is clear that the internal mammary artery offers several potential advantages over standard palliative shunts and can be used successfully to treat cyanotic heart disease in selected cases. It is important to carefully review the preoperative angiogram to define as precisely as possible the anatomy and size of the internal mammary artery and the mediastinal collaterals that provide pulmonary blood flow. In addition, the surgeon should inspect the internal mammary artery during thoracic exploration in preparation for a standard or modified Blalock-Taussig shunt. We believe that this shunt may be the procedure of choice in the occasional older child with an internal mammary artery large enough to allow a satisfactory anastomosis to the pulmonary artery.

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Use of a New Stapling Instrument for Permanent Occlusion of the Aorta in the Surgical Procedure for Thromboexclusion

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Permanent aortic occlusion is required in the surgical procedures for the flow reversal and thromboexclusion technique and also for the permanent exclusion of aneurysms of the thoracic aorta. We have designed a stapling instrument for the permanent occlusion of the aorta and have used it in 5 patients with aortic dissections and 2 patients with aneurysms of the thoracic aorta. This report describes our newly designed surgical stapler for the closure of the aorta with 2 case reports.

(Ann Thorac Surg 1989;47:466–9)

In the past few decades, many stapling instruments have been developed and widely used for the autosuture of the lungs or gastrointestinal tract [1, 2]. Moreover, staplers were recently applied in operations for aneurysms of the aorta [3]. However, almost none of the staplers are designed for the autosuture of the aorta.

In this paper, we introduce our newly developed stapling instrument (Takasago Medical Instrument Company, Tokyo, Japan) and our operative method for permanent closure of the aorta with 2 case reports.

The Stapler and Staples

The stapler and staples are shown in Figure 1. The staples are 0.5 mm in cross-sectional diameter, 7 mm in width, and 7 mm in limb length. In our fundamental studies using mongrel dogs, severe impairment of the aortic wall was pathologically evident if the closed staple height was less than 2 mm using any stapler [4]. Our stapler was designed to obtain a closed staple height of slightly less than 3 mm after complete stapling.

The jaws of the stapler are 7 cm long. The cartridge housing can load a double staggered row of 14 stainless steel staples. The staples are pressed on three separate parts of the cartridge housing to obtain secure and powerful stapling.

The staple line of the aortic arch was buttressed with a thick sheet of USCI double velour Dacron fabric to reinforce the friable aortic wall. (A thick Dacron felt was too hard for stapling.)

Jaw C1 (see Fig 1) is inserted behind the posterior wall of the aortic arch. Then, handles B2 and C2 are grasped for aortic clamping. Finally, handles A2 and C2 are pressed for aortic stapling. As a final procedure, staples are pressed on the three separate parts of the cartridge housing to obtain secure and powerful stapling.

Operative Method

The operation was carried out through a median sternotomy and midline abdominal incision with extension to the left neck. A woven Dacron graft (about 20 mm in diameter) was bypassed from the ascending aorta to the infrarenal abdominal aorta as described by Carpentier and associates [5]. Then, an 8-mm Dacron graft was implanted on the aortic bypass graft for the revascularization of the left subclavian artery. A double velour Dacron fabric was encircled around the aortic arch at the origin of the left subclavian artery. Finally, the aortic arch was stapled by our stapler (Fig 2). The aortic arch was sandwiched between the Dacron fabric and a double row of staples.

Case Reports

Patient 1

A 54-year-old man was referred to our hospital for evaluation of chest pain and transient attacks of vertigo. He had an antecedent episode of severe back pain 9 months before admission. He also had a history of hypertension for 4 years and had sustained a cerebral infarction 6 months before admission.

On admission, his pulse rate was 84 beats per minute and his blood pressure was 132/100 mm Hg. A chest roentgenogram demonstrated aneurysmal dilation of the distal aortic arch. Electrocardiogram showed left ventricular hypertrophy. Preoperative digital subtraction angiography demonstrated DeBakey IIIb dissection associated with aneurysmal dilation of the distal aortic arch and stenosis of the true lumen.

Operation was carried out through a median sternotomy and midline laparotomy with extension to the left neck to provide wide exposure of the aortic arch and its

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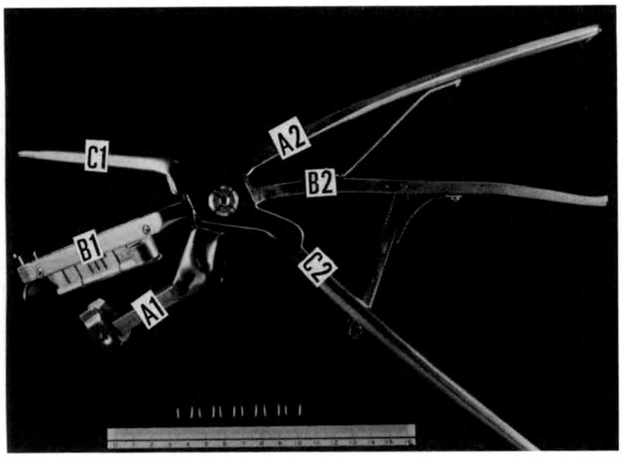

Fig 1. Our stapler and the staples (shown at the bottom of the figure). Each part of the stapler is indicated by the marked labels, as discussed in the text. B1 *is the cartridge housing.*

branches. After a 20-mm woven Dacron graft was bypassed between the ascending aorta and infrarenal abdominal aorta, the left subclavian artery was divided and connected to an 8-mm woven Dacron graft, which was anastomosed to the 20-mm graft. Then, double velour Dacron fabric was encircled around the aortic arch at its takeoff from the left subclavian artery. Finally, the aortic arch was stapled by our stapler without substantial bleeding (Fig 3).

Digital subtraction angiogram 6 months after operation showed complete occlusion of the aortic arch and excellent patency of all bypassed grafts (Fig 4).

Patient 2

A 58-year-old man who had a history of hypertension for 10 years noticed sudden onset of intermittent claudication 3 months before admission. He had also suffered from a cerebral infarction 10 years earlier.

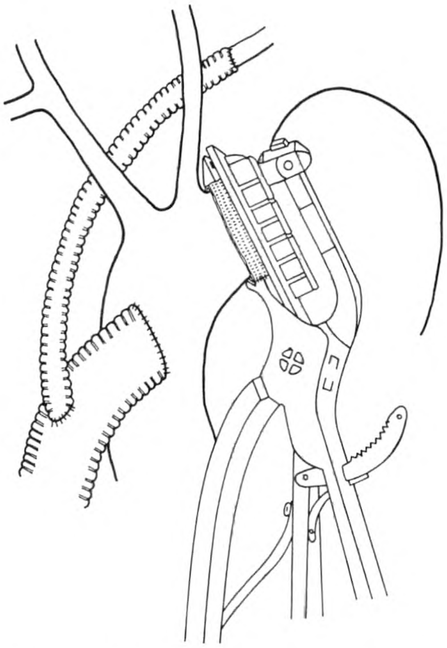

Fig 2. Our operative method using the stapler. The aortic arch is stapled at the origin of the left subclavian artery.

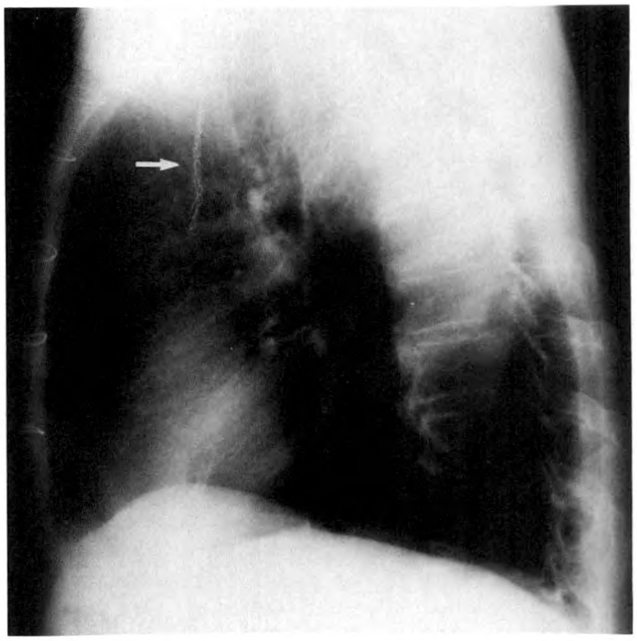

Fig 3. Postoperative chest roentgenogram of patient 1 (lateral view). The white arrow *indicates the staple line.*

He was admitted because of progression of intermittent claudication. His blood pressures on the right arm and right ankle were 144/82 mm Hg and 104/60 mm Hg, respectively.

Digital subtraction angiogram demonstrated a DeBakey IIIb dissecting aortic aneurysm arising from the distal aortic arch to the juxtarenal abdominal aorta and associated with a tiny abdominal aortic aneurysm and tight stenosis of the left renal artery.

Operation was carried out through a median laparotomy. After the tiny aneurysm of the abdominal aorta was replaced with an 18-mm woven Dacron graft, the ascending aorta and the aortic arch and its branches were exposed through a median sternotomy. A 20-mm woven Dacron graft was inserted for bypass from the ascending aorta to the graft that was previously interposed in the abdominal aorta. Then, two 8-mm grafts were bypassed from the ascending aorta–abdominal aorta bypass to the divided left subclavian artery and left renal artery, respectively.

Next, the aortic arch was encircled with double velour Dacron fabric at the origin of the left subclavian artery. Finally, the aortic arch was stapled by our stapler under pharmacologically induced hypotension.

Digital subtraction angiogram 2 months after operation demonstrated complete occlusion of the aortic arch and excellent patency of all bypass grafts (Fig 5). Postoperative computed body tomogram showed massive thrombus formation in the dissected false lumen.

Comment

Recently, Carpentier's flow reversal and thromboexclusion technique has been widely used as one of the surgical procedures for dissecting aortic aneurysm [5]. We think this procedure is a fundamentally palliative operation for the surgical treatment of dissecting aortic aneurysms. However, many surgeons have experienced technical difficulties in permanently occluding the aorta just distal to the origin of the left subclavian artery.

We consider the stapling of the aortic arch at the origin of the left subclavian artery to be safer and easier than at the origin of the distal aortic arch. The reason we choose this location for stapling is that we would like to staple the aorta at a site free from friable dissecting disorder and under safer vision.

Permanent aortic occlusion is also required in the surgical procedure of ascending aorta to abdominal aorta bypass and complete exclusion or resection of aneurysms of the descending thoracic aorta [6, 7].

Methods of aortic occlusion include (1) manual suturing under temporary aortic clamp, (2) permanent aortic clamp, and (3) stapling. The first method is a time-consuming procedure. Furthermore, it may be hazardous for loose ligations under temporary aortic clamp.

Using the second method, Carpentier has applied his originally developed aortic clamp for this purpose. However, we think this clamp is too bulky and may compress the surrounding tissues such as the pulmonary artery or bronchus. Furthermore, it may also be difficult to release the clamp if the clamping was not satisfactory.

Regarding the last method, the cartridge housing seems to be very bulky for smooth and safe placement of the stapler around the aorta just distal to the left subclavian artery, even if a flexible stapler were used.

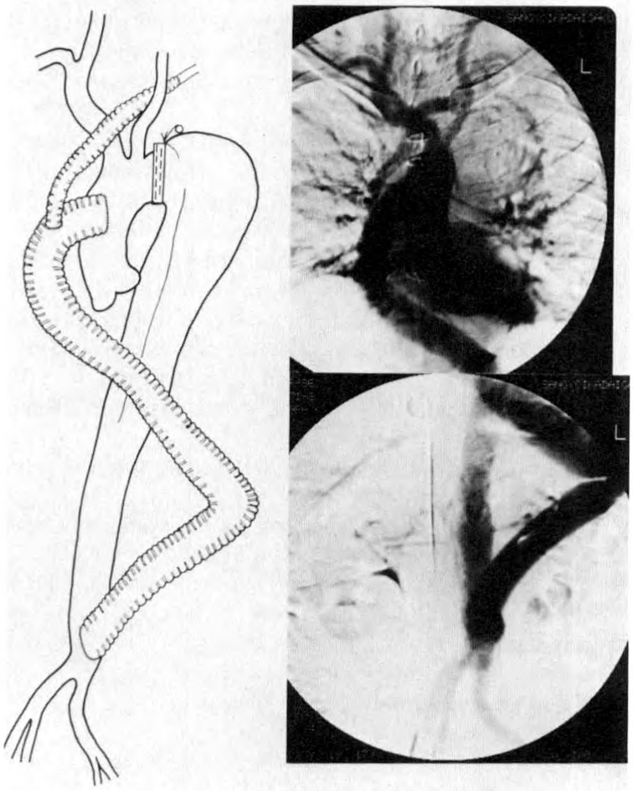

Fig 4. The operative method and the postoperative digital subtraction angiogram of patient 1.

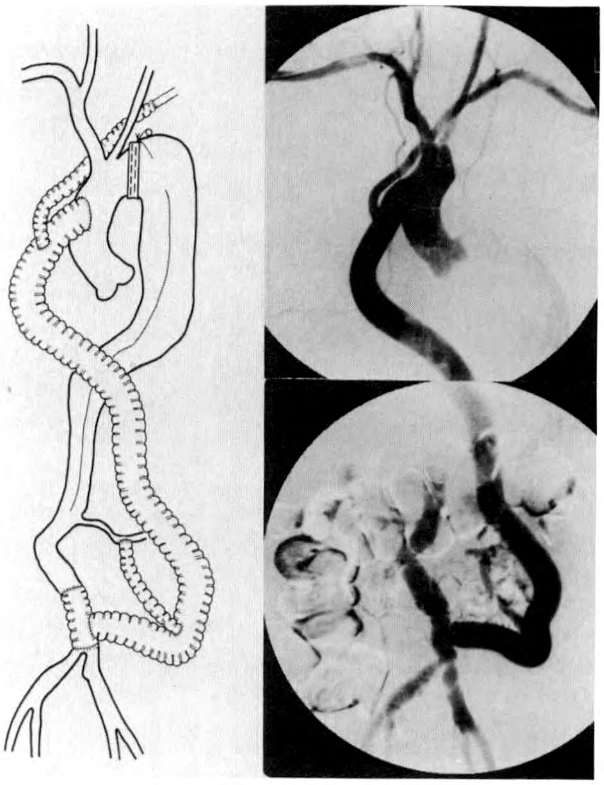

Fig 5. The operative method and the postoperative digital subtraction angiogram of patient 2.

Universally available staplers are mainly made for use in pulmonary and gastrointestinal operations. Furthermore, almost all of the staplers are designed for a closed staple height of less than 2.5 mm. These staplers cannot make B-shaped staples if the closed staple height is greater than 2.5 mm. For the purpose of buttressing the staple line in the aorta with double velour Dacron fabric, 2 mm of closed staple height is considered to be hazardous. We conclude that complete stapling can be obtained with less impairment to the aortic wall if the closed staple height is a little less than 3 mm.

To gain sure and powerful stapling, the cartridge housing of our stapler is divided into three parts and staples are pressed in three steps. We are not sure how to prevent bleeding from a staple line if a Dacron sleeve is not used. We believe that the use of a Dacron sleeve allows safer stapling, and therefore we do not intend to perform aortic stapling without a Dacron sleeve. In all cases, proximal closure of the aorta was accomplished completely without substantial bleeding. Furthermore, there was no nerve or carotid injury after closure of the aorta at the origin of the left subclavian artery.

We have already applied this instrument for treating 5 cases of dissecting aortic aneurysm and 2 cases of thoracic aortic aneurysm. Operative methods for the former 5 patients included Carpentier's flow reversal and thromboexclusion technique, and for the latter 2 patients, permanent ascending aorta to abdominal aorta bypass and complete exclusion of the aneurysm (Table 1).

There were no cases of intraoperative death. There was

Table 1. Use of Aortic Stapling in 7 Patients

Patient	Age (yr)	Sex	Type of Aneurysm	Operative Procedure	Follow-up	Complications	Outcome
1	50	M	IIIb	TE	5 years	Paraplegia	Alive
2	82	M	IIIb	TE	3 months	Fulminant hepatitis	Late death
3	63	M	IIIb	TE + graft replacement of AAA	4 weeks	Sepsis	Operative death
4[a]	54	M	IIIb	TE	3 years	. . .	Alive
5	56	M	Takayasu's arteritis	Exclusion of aneurysm	3 years	. . .	Alive
6[b]	58	M	IIIb	TE + graft replacement of AAA + left renal artery bypass	2 years	. . .	Alive
7	60	M	Pseudoaneurysm of aortic arch	Exclusion of aneurysm	3 months	Cerebrovascular accident	Late death

[a] This is the patient presented in the first case report. [b] This is the patient presented in the second case report.

AAA = abdominal aortic aneurysm; TE = thromboexclusion.

1 death 4 weeks postoperatively, caused by septicemia after bone marrow arrest due to antibiotics. The follow-up periods of the other 6 patients ranged from 3 months to 5 years. There were 2 late deaths 3 months after operation due to fulminant hepatitis and a cerebrovascular accident, respectively. Paraplegia occurred in 1 man who required division of the descending thoracic aorta at the level of T-8, because of rupture of the distal aortic aneurysm on the day of the operation. Four patients are currently alive after postoperative periods of 2 to 5 years (Table 1).

The advantages of our stapler and operative method are as follows. (1) Use of the stapler allows rapid occlusion of the aorta without substantial bleeding. (2) Our stapler provides less impairment of the aortic wall than those currently available, because it is designed to obtain a closed staple height of a little less than 3 mm. (3) The aortic arch at the origin of the left subclavian artery provides a safer and more secure occlusion site than the distal aortic arch, in which the dissecting disorders are involved.

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Angiocatheter Coronary Artery Reperfusion Before Cardioplegia for Evolving Myocardial Infarction

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A simple reperfusion method using an angiocatheter during total cardiopulmonary bypass before aortic cross-clamping is described. This method has been used successfully for catastrophic evolving myocardial infarctions.

(Ann Thorac Surg 1989;47:470–1)

Emergency operation for an evolving myocardial infarction with superimposing global ischemia during aortic cross-clamping may result in additional infarct extension, even though the myocardium is protected with cardioplegic solution. It has been experimentally proved that this infarct extension can be prevented by reperfusing the ischemic zone before aortic cross-clamping [1]. We describe a simple method for flow reestablishment to the obstructed coronary artery before aortic cross-clamping during cardiopulmonary bypass (CPB).

Material and Methods

After the establishment of total CPB, a 20-gauge Teflon angiocatheter is inserted into the critically obstructed coronary artery or obstructed saphenous vein graft (Fig 1). It is then connected to an extension tube (internal diameter, 2.5 mm), with an 18-gauge needle on the proximal end of the tube inserted into the perfusion line. This circuit is perfused by the same 37°C blood as the systemic circulation, and bidirectional flow inside of the coronary artery can be expected. The flow rates of this circuit depend on the CPB flow. In our experience, at a CPB perfusion pressure of 50 mm Hg, the free flow was 42, 60, and 67 mL/min during a systemic CPB flow of 4.0, 5.0, and 5.5 L/min, respectively. Insertion of the angiocatheter into a coronary vessel is not difficult if the ventricle is decompressed, weakly beating, or fibrillating during total bypass. We believe all large coronary arteries (2 mm or greater) could easily be cannulated this way unless they are diffusely diseased or total thrombosis of the vessel is detected.

During the reperfusion period of 20 to 30 minutes, the saphenous vein or the internal mammary arteries are harvested and the aortic anastomosis for vein grafting can be constructed. The aorta is then cross-clamped, cardioplegia is given, and the distal anastomoses are performed. The site of the temporary reperfusion technique can be a point for a distal anastomosis on a coronary artery.

Another benefit of this technique is to deliver cardioplegic solution through this circuit into the obstructed coronary artery if the myocardium cannot be cooled through the aortic root injection. We observed in 1 patient a rapid drop of myocardial temperature in the region of the obstructed coronary artery to 10°C after injection of 200 mL of cardioplegic solution through this circuit. Before this selective injection, the myocardial temperature stayed at 26°C after the delivery of 1000 mL of cardioplegic solution through the aortic root.

Comment

Various nonsurgical reperfusion methods for acute myocardial infarction, such as percutaneous transluminal coronary angioplasty, thrombolysis, or use of a reperfusion catheter with multiple sideholes for acute coronary occlusion during percutaneous transluminal coronary angioplasty [2], are being used clinically. These methods do not decompress the ventricle, which may be necessary to save a substantial amount of myocardium [3]. It may also be impossible to apply these techniques to a catastrophic ischemic event if the patient does not respond to the immediate initiation of cardiopulmonary resuscitation. Hemodynamic assist using CPB and emergent surgical revascularization may be the only way to save these patients. The method we describe here will not only decompress the ventricle, but will also rapidly reperfuse the critical segment of myocardium before global ischemic arrest from cardioplegia.

Horneffer and associates [1] experimentally demonstrated that superimposing global ischemia on a heart during an evolving myocardial infarction resulted in additional infarction even though myocardial protection with hypothermic single-dose cardioplegia was used. This infarct extension could be completely prevented by reperfusing the ischemic zone before inducing global ischemic arrest. We have clinically applied this principle successfully in 3 patients. The ischemic events were cardiac arrests after coronary angiography for left main coronary artery disease in 2 patients and during the dissection of old saphenous vein grafts in a reoperation for coronary artery disease in 1 patient. The time from their arrests to the initiation of ventricular decompression using CPB and temporary reperfusion was 15 to 25 minutes. Within five

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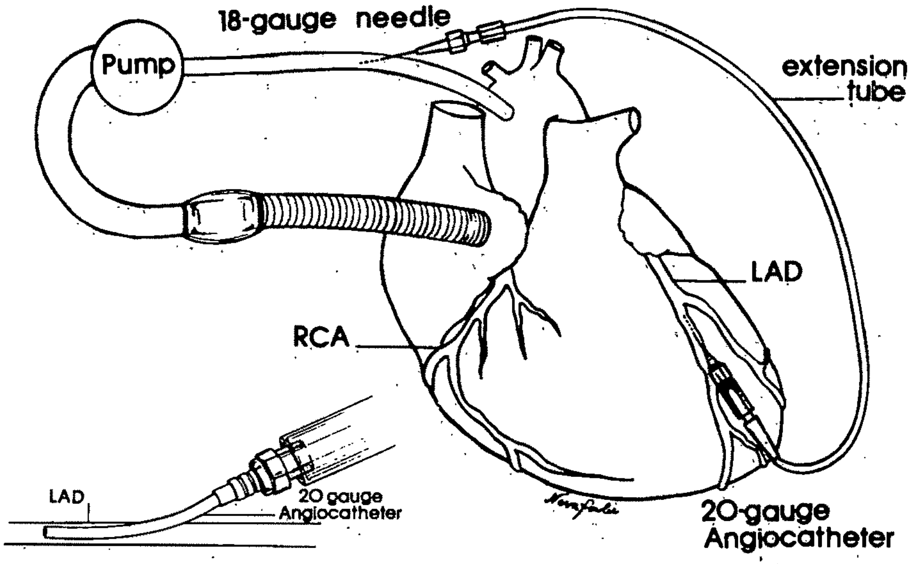

Fig 1. A 20-gauge angiocatheter is inserted into the left anterior descending coronary artery (LAD) and then connected to an extension tube. An 18-gauge needle on the proximal end of the tube is then inserted into the cardiopulmonary bypass perfusion line. (RCA = right coronary artery.)

minutes after the reperfusion, we observed the hearts in all 3 patients to resume good contractility, and the elevated S-T segments returned to baseline. These patients survived without electrocardiographic evidence of perioperative myocardial infarction.

We thank Neva Fowler for the illustration and Dixie Van Syoc and Janet Emerick for preparation of the manuscript.

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Is the Shunt Patent?

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A novel technique for auscultating an aortopulmonary shunt murmur utilizing the principle of conduction of sounds through a closed air system is described.

(Ann Thorac Surg 1989;47:472)

The principle of the conduction of heart sounds and murmurs through an air column for auscultation was popularized by Laennec and Theophile [1] and resulted in the modern stethoscope. This allows selective, enhanced auscultation of cardiac events. Another application of this principle is the esophageal stethoscope much used by pediatric anesthetists.

We have made an interesting, if obvious, observation that utilizes this principle in assessing the patency of systemic–pulmonary artery shunts, specifically, the Blalock-Taussig shunt and its modified form. Anxiety regarding the patency of a shunt is common in the early postoperative period; this is due to varying saturations, respiratory variables, hemodynamic lability, and, often, difficulty in auscultating the shunt murmur.

The ideal in systemic–pulmonary artery shunts is early extubation, but in our experience the infants are often intubated for at least 18 to 24 hours. During this period the shunt can be reliably auscultated by disconnecting the endotracheal tube from the ventilator and applying, occlusively, the bell of a stethoscope to the open endotracheal tube connection briefly during a quiescent phase of respiration (Fig 1). Because of the proximity of the shunt to the major airways, the trachea and bronchi, and the excellent conduction of the sound by the air column, the shunt murmur is often well heard by comparison with precordial auscultation, or audible when it is not so by standard auscultation.

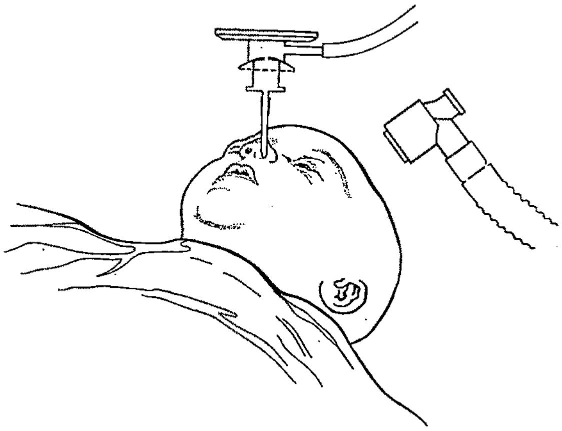

Fig 1. The bell of the stethoscope is applied occlusively to the open endotracheal tube connection.

It is recommended that after intubation in the operating room, and before operation, auscultation be performed to establish a baseline, as a ductal shunt murmur or collateral flow murmur may be present. Auscultation is again done at the end of the procedure and periodically in the intensive care unit to confirm patency.

We have found this an extremely useful and reassuring sign over the past 2 years, and recommend its use as an adjunct in assessing the status of the uncertain shunt.

To our knowledge, this is an original observation. Its application could be extended to monitor the status of the ductal shunt in other situations of congenital heart disease and in neonates with persistent respiratory distress syndrome due to a patent ductus arteriosus.

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Sutureless Fixation of Long Aortocoronary Saphenous Vein Grafts With Oxidized Regenerated Cellulose

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A technique of sutureless epicardial fixation of long aortocoronary saphenous vein grafts using oxidized regenerated cellulose is illustrated. Sutureless fixation has been previously performed with fibrin glue. Possible advantages of using oxidized regenerated cellulose instead of fibrin glue are discussed.

(Ann Thorac Surg 1989;47:473–4)

Adequate routing of long aortocoronary saphenous vein grafts (SVGs) has been traditionally achieved by fixing the graft in proper position by means of fine adventitia–epicardium sutures. Sutureless fixation using fibrin glue has been proposed [1]. We report a simple technique using oxidized regenerated cellulose (ORC).

Material and Methods

With the patient off cardiopulmonary bypass and after completion of hemostasis, an ORC sheet of adequate size is tailored. While the first assistant holds the SVG in the proper position, the sheet is laid loosely over the segment of graft the surgeon wants to hold in place (Fig 1). The area should be moistened with some blood, but soaking should be avoided as it would hinder adhesion of the ORC sheet.

Excessive length of an SVG reaching the left coronary system through the transverse sinus can be compensated for by looping the extra length in the aorta–right atrial groove (Figs 2A, 2B). To achieve this, it is essential that the axis of the proximal anastomosis be at a very narrow angle with the long axis of the ascending aorta. An ORC sheet is placed over the loop to fix it in position (Fig 2C).

Occasionally a graft reaching the left coronary system after being routed over the pulmonary artery is pushed and kinked by a hyperinflated left lung. To obviate for this, a horizontal incision is made in the pericardium where this touches the graft and the subpleural fat is exposed. After the SVG has been routed appropriately, an ORC sheet is placed and the pericardium roofed over to make the subpleural fat cover the graft (Fig 3). The ORC will adhere to both the SVG and the fat. Additional immobilization may be obtained by tacking the medial edge of the pericardium to the aortic root or pulmonary artery adventitia.

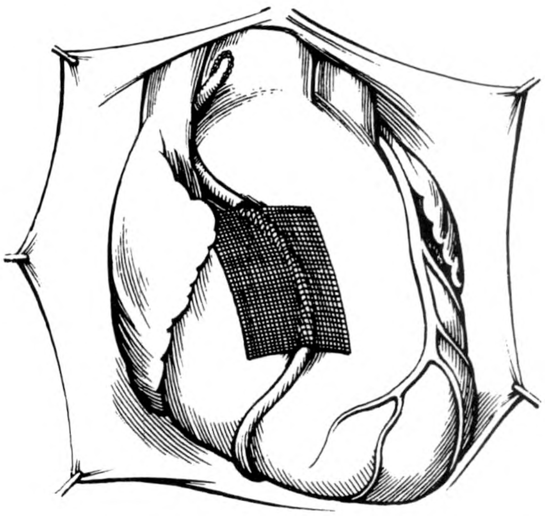

Fig 1. The graft to the right coronary artery is accommodated over the right ventricle in a lazy-S fashion and kept in place with an oxidized regenerated cellulose sheet.

Comment

Fixation of an aortocoronary SVG by means of a suture is often troublesome, because the point of fixation may represent a hinge and the graft may kink elsewhere. Besides, constriction or damage of a small and thin-walled vein (eg, arm vein) may occur.

Fibrin glue has been used for sutureless fixation [1]. Oxidized regenerated cellulose, widely used as a topical hemostat and commercially available as a loose knit (Johnson & Johnson Products, Inc, New Brunswick, NJ), may be a valid alternative for the following reasons.

1. The ORC sheet readily adheres to a surface moistened with blood and conforms its shape to the surface it covers. The sheet, however, loses its adhesiveness if soaked by excessive, poorly clotting blood.

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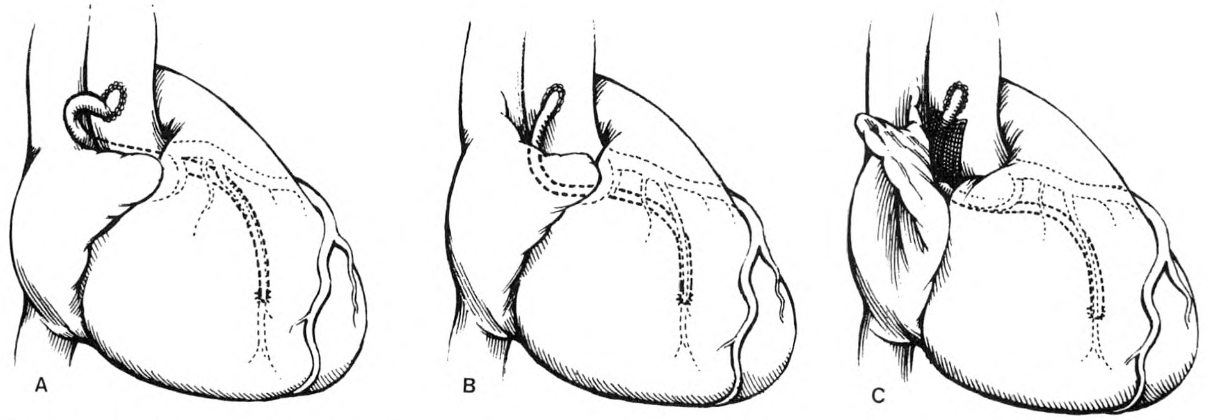

Fig 2. An extra length of graft causes a kink close to the proximal anastomosis (A). A loop is formed in the aorta–right atrial groove (B) and fixed in position with an oxidized regenerated cellulose sheet (C).

2. Oxidized regenerated cellulose is rapidly degraded and is accompanied by only a mild tissue reaction. As a matter of fact, some experimental work shows its propensity toward producing a graded reduction in peritoneal adhesion formation [2]. The reason that the tissue reaction is mild may be that ORC is absent in the final phase of the healing process involving fibroblast proliferation. Only two instances of vascular stenosis have been reported; in those cases wrapping of the ORC sheet was performed (data on file, Johnson & Johnson Research). In our technique the sheet is placed loosely over the SVG.
3. Oxidized regenerated cellulose has definite bactericidal properties deriving from its low pH [3]. This is an advantage over fibrin glue, with its low but existing risk of disease transmission related to its fibrinogen content.
4. The cost of ORC is definitely less than that of fibrin glue. A 2-inch by 3-inch sheet is sufficient for the purpose, whereas most of the fibrin glue, made from 25 to 50 mL of cryoprecipitate and 5 mL of thrombin, remains unused [4].

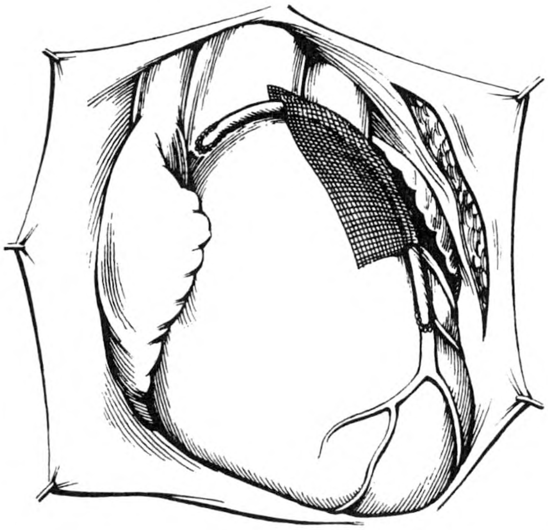

Fig 3. To avoid pushing and kinking of the graft by a hyperinflated lung, the pericardium is divided, an oxidized regenerated cellulose sheet is placed on the graft, and the subpleural fat is apposed on it for immobilization.

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In the Beginning

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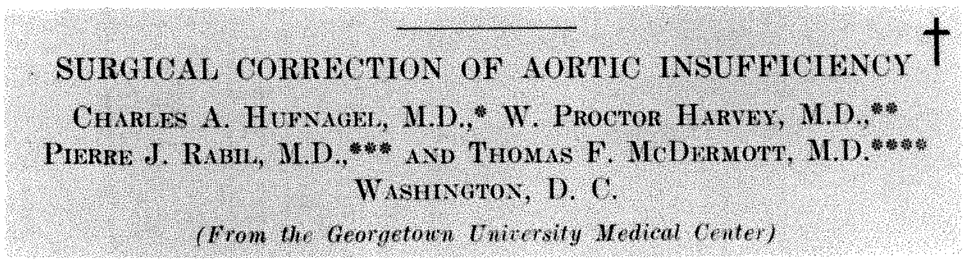

SURGICAL CORRECTION OF AORTIC INSUFFICIENCY †

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PIERRE J. RABIL, M.D.,*** AND THOMAS F. McDERMOTT, M.D.****
WASHINGTON, D. C.

(From the Georgetown University Medical Center)

It all began with the reinvestigation of isografts in the experimental laboratory. The background of the legacy of Carrel had been all but forgotten and had had little clinical application because of the logistical problems of maintaining a proper supply of sizes and paucity of satisfactory methods of preservation of blood vessels, as well as a lack of confidence that these arteries could function for long. My colleagues and I evolved a method for the rapid freezing of arteries taken aseptically first from animals and then from cadavers, which, though not alive, functioned and could be stored at −70°C for months. This rapidly evolved into a freeze drying process with storage in a vacuum for even greater ease of procurement and sterilization with liquid ethylene oxide.

While these trials with isografts were proceeding it was evident that they were merely structural conduits that were well tolerated as arterial replacements. Although all of Carrel's attempts at substitution of nonbiological materials had not been successful, it appeared worthwhile to renew this investigation with some of the more recent polymeric materials then available. After numerous trials by implantation to determine the biological degrees of reactivity, body fluid absorption, and biodegradability, basic criteria were established as desirable for an intravascular implant.

Methyl methacrylate was chosen for the first experiments, and 5-cm-long tubes 1 cm in diameter were machined from solid blocks of the polymer. After the material was shaped into tubes, small grooves were placed at each end. I polished the inside of each tube to a very smooth surface and then repeatedly cleaned all the surfaces to eliminate residual extraneous materials.

Fixation of a rigid tube in the thoracic aorta remained a major problem. Circumferential ligatures usually produced necrosis of the normal aorta beneath the ligature and massive hemorrhage resulted after a few days. To overcome this the principle of "multiple-point fixation" was conceived. A semiflexible ring of nylon was devised that had blunted teeth, an inside diameter 1 mm larger than the depth of the groove of the tube, and spaces between the teeth, which maintained the blood supply to the distal aortic cuff (Fig 1). The body of the rings did not touch the aorta when it was closed. In this way the rings held the aortic wall securely but did not initiate necrosis or permit slipping or bleeding once the ring was fixed in position.

These later experiments allowed us for the first time to replace the thoracic aorta with nonbiological material and to maintain predictable patency. Once the use of the methacrylate tube was demonstrated, the concept of modifiying the tube to a valve was quite evident, but many questions remained unanswered. What kind of valve? Will it produce clotting? How will it wear? Will it break? Can it always fully open and fully close?

Many different types of valves were tested. The free floating ball was finally chosen for extensive animal testing. The solid methacrylate ball was too heavy, so it was made hollow to give it a specific gravity of 1. The chamber for the ball provided an area around the ball for passage of blood that was one and a half times the area of the inlet and outlet, so that there was no pressure drop across the device. As the ball needed stops in the direction of forward flow and to seat fully in the other direction, the chamber was made in two pieces. The stops were fixed in one half and the ball placed in the other. Then the step flanged halves were exactly matched, locked, and sealed from the outside.

Although many of the experimental results with these hand-made models were successful improvements, we continued to seek and find more and more refinements. The production of a single shell containing the hollow methacrylate ball was made by Carl Hewson of the Brunswick Mfg Co using pressure vacuum forming methods, which gave a smooth surface with indentations for stops in the open position (Fig 2). This decreased our concern over separation of the chamber over a long time.

The results in the laboratory demonstrated the efficacy of the valve and patency in the thoracic aorta, but the opening and closing of the valve made a readily audible

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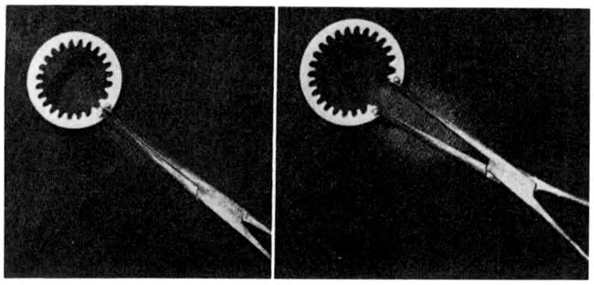

A B

Fig 1. The ring-holding instrument, shown in the closed (A) and open (B) positions.

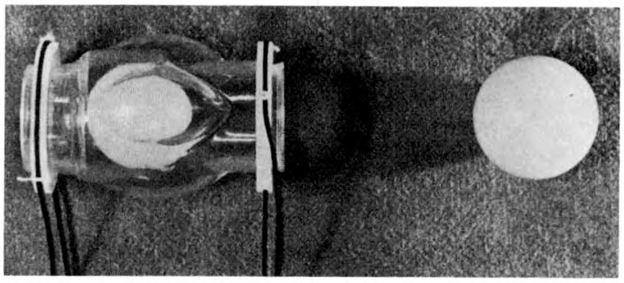

Fig 2. The assembled one-piece valve (left) is shown with the multiple-point fixation rings in place in the grooves of the valve. The smooth surface of the polyethylene ball is demonstrated at the right, before assembly in the valve chamber.

noise. This noise was discussed with the patients at length before operation, and it is interesting that none refused operation for this reason, or felt that it was a real problem after operation. The first operation was performed in October of 1952 with survival of the patient for many years.

After operation on the first few patients, the hollow methacrylate ball was changed to one with a nylon core covered with a 5-mm layer of silicone elastomere cured by heat and high pressure. This markedly reduced the noise and maintained the specific gravity of blood for effectiveness and wearability. To my knowledge there were no failures due to valvular dysfunction of mechanical valve origin. The thrombotic phenomena encountered were also seen for a long period with later valves in intracardiac positions. As most of the patients who had these valves had advanced myocardial disease from their valvular defects, and many were beyond middle age when operated on, there were relatively few who survived for more than 10 years without the need for reoperation. The valve in the descending aorta did not control all of the regurgitation. It was foreseen that replacement in the normal position was probable in the near future, and that it would not require the removal of a prosthesis placed in the descending aorta. Valves have been recovered from patients 30 years after implantation that have not shown major changes due to wear or any impairment of function of the prosthesis. It is of note that the successful demonstration of the usefulness of this device has been father to a veritable host of polymer-biological related industries and applications.

Primary Small Cell Carcinoma of the Esophagus

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A primary small cell carcinoma of the esophagus in a 61-year-old woman was treated by transhiatal esophagectomy. The clinical data were correlated with data obtained from a review of the 129 cases reported in the world literature, thereby providing a clinical profile and suggested management strategy for this rare type of esophageal malignancy. Presenting symptoms of esophageal small cell carcinoma include dysphagia (75.3%), weight loss (38.4%), and chest pain (23.3%). Treatment regimens have included surgical intervention in 58%, radiotherapy in 10%, chemotherapy in 6%, or some combination of these in 26%. Overall survival is only 20.7 weeks after diagnosis. The fact that three fourths of affected patients had metastatic disease at the time of diagnosis leads us to recommend surgical intervention plus systemic chemotherapy in these patients.

(Ann Thorac Surg 1989;47:477–80)

Small cell carcinomas (SCCs), also known as oat cell carcinomas, are aggressive tumors most frequently described in the bronchial tree. They present both diagnostic and therapeutic problems. Initially they must be differentiated from lymphomas and sarcomas of similar cell size, and subsequently their presence must be identified as primary or metastatic. Primary SCCs have been described in numerous extrapulmonary sites, including the breast, uterine cervix, and virtually all regions of the aerodigestive tract [1].

The cellular origins of SCC have been the subject of intense speculation and debate. Based on morphological and histochemical similarities between SCC tumor cells and peptide-secreting endocrine cells, a primitive multipotential endocrine cell has been postulated as a source [1–3]. These primitive endocrine cells, possibly originating from the neural crest, possess the ability to synthesize and store amines as well as to decarboxylate certain amino acids to form biologically active amines. This has led to the terminology of APUD (amine precursor uptake, decarboxylase) cells as proposed by Pearse [3]. Primitive APUD neural crest cells are thought to migrate into the fetal aerodigestive tract. Although the cellular origins of SCC are controversial, APUD cells are found in normal human esophageal mucosa [4].

Extrapulmonary SCCs are uncommon malignancies, unlike pulmonary SCCs, which make up approximately 20% of all lung cancers [1]. There is little available information concerning the clinical courses or the responsiveness to treatment of this group of tumors. McKeown [5] is credited with one of the first reports of extrapulmonary SCC, having described in 1952 2 cases of SCC of the esophagus out of more than 9,000 autopsy specimens. Since that report, a variety of extrapulmonary SCCs have been described and reviewed [1, 6]. We collected the available data on 129 cases of SCC of the esophagus in the world literature for review and analysis.

Material and Methods

The clinicopathological correlates of esophageal SCC have not been defined clearly in the surgical literature because most reports have been isolated clinical or pathological reviews of a single tumor or small series. The purpose of this review is to collect all evaluable data from the 129 patients with esophageal SCC reported in the literature and from our personal experience to develop an accurate clinical profile and management strategy.

Case Report

To illustrate one clinical approach to this tumor, the case of a patient with a primary SCC of the esophagus is presented. This 61-year-old woman was seen at The Johns Hopkins Hospital in April 1987 with a 2-year history of chest pain and mild dysphagia. The patient had undergone a barium esophagogram and cardiac evaluation approximately 18 months previously, which failed to disclose any abnormality. She denied any weight loss, gastroesophageal reflux symptoms, or fever. Physical examination revealed a well-appearing, mildly obese woman. Examination of the chest, abdomen, and lymph node–bearing areas was unremarkable. Admission blood studies were all normal. A computed tomographic scan of the chest and abdomen revealed a 6-cm mass in the midesophagus with a small left paraaortic lymphadenopathy. Esophagogastroduodenoscopy demonstrated an ulcerated polypoid mass in the midesophagus, 26 cm from the incisors, that filled approximately half of the esophageal lumen. Biopsy specimens revealed SCC of the esophagus.

In May 1987, the patient underwent a transhiatal esophagectomy with cervical esophagogastrostomy, cholecystectomy, and feeding jejunostomy. The postoperative course was complicated by an anastomotic leak, which was treated by open drainage, and a left chylothorax, which resolved with tube thoracostomy drainage and hyperalimentation. The patient was discharged home on the 35th postoperative day. She could tolerate a regular

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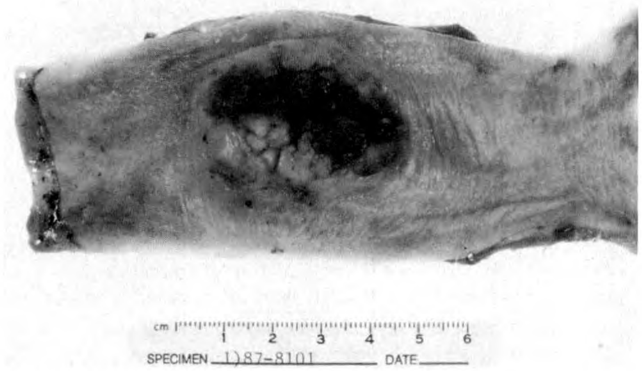

Fig 1. Ulcerated small cell carcinoma of midesophagus.

diet and had refused adjuvant chemotherapy. One month after discharge, the patient moved to another state and was lost to follow-up.

Pathological examination revealed a 4.4 × 3-cm raised, ulcerated midesophageal lesion extending to the deep margins of the specimen (Figs 1, 2). Microscopically the tumor showed in situ and infiltrating carcinoma with predominantly a small cell undifferentiated appearance and focal areas of squamous differentiation (Fig 3). Metastatic tumor was present in two periesophageal lymph nodes and a left gastric lymph node. Mucosal margins were negative for tumor.

Review of Literature With Clinicopathological Correlations

Including the index case, a total of 130 cases of SCC of the esophagus were reviewed [5, 7–43]. Available clinicopathological information was gathered from each reference to create summary statistics. Of the 130 patients, 61.4% were male and 38.6% were female. The mean age was 64 years (range, 29 to 88 years). The principal symptoms were dysphagia (75.3%), weight loss (38.4%), and chest pain (23.3%), and the mean duration of symptoms was 4.4 months. It is apparent that the presenting signs and symptoms are similar to those of patients with other, more common histological types of esophageal cancer. Ectopic endocrinopathic findings were noted in 2 patients [14, 27]. A history of alcohol or tobacco use was mentioned for very few patients and was not evaluable etiologically.

Tumor characteristics are summarized in Table 1. Squamous cell carcinoma of the esophagus is typically diagnosed at an advanced, metastatic stage with bulky primary tumors present. Components of SCC were seen in 23.2% of patients, including the index patient, in whom squamous cell carcinoma was found at the time of preoperative endoscopic biopsy. Glandular elements were reported in 4 patients, and 3 tumors showed carcinoid differentiation [32]. Multiple esophageal carcinomas were reported in 2 patients [22, 30]. Argyrophilia is seen in 15% to 50% of pulmonary oat cell carcinomas [15, 44], and was found in 56% of esophageal SCCs [9–15, 18, 19, 21, 23, 25, 27, 28, 35]. Cytoplasmic argyrophilia is not considered essential for diagnosis [25, 27]. The presence of dense-core granules on electron microscopic examination is important, but not essential for diagnosis [15, 25, 27]. Electron-dense granules characterize SCC of the lung [15, 45], and were found in 66% of esophageal SCCs [10–15, 18–21, 25, 28, 32–35]. The absence of a primary pulmonary SCC was documented in all reported cases of esophageal SCC.

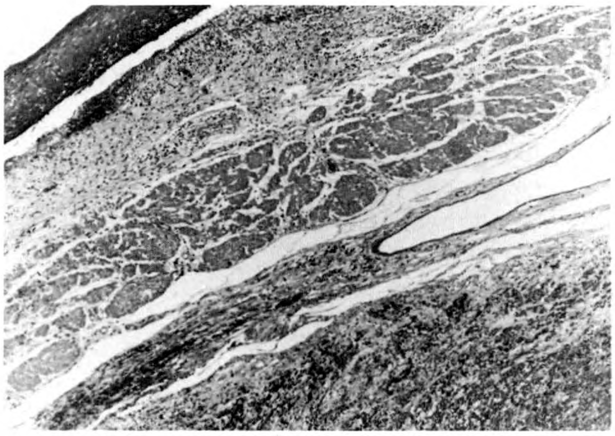

Fig 2. Low-power view of small cell carcinoma of esophagus showing invasion through wall of esophagus. (H & E; ×10 before 51% reduction.)

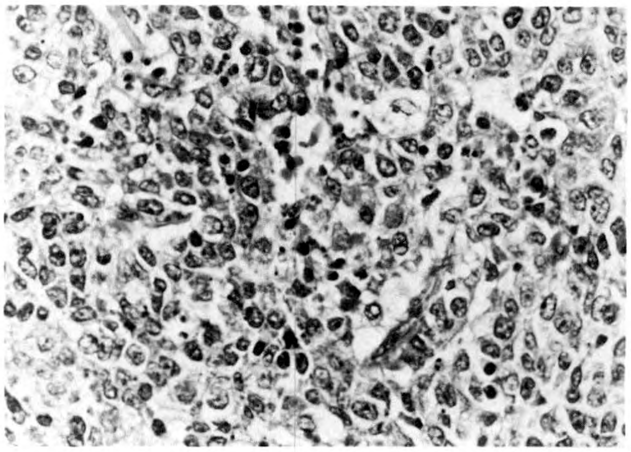

Fig 3. Small cell pattern of esophageal tumor showing hyperchromatic or vesicular nuclei (H & E; ×740 before 50% reduction.)

Table 1. Tumor Characteristics of Esophageal Small Cell Carcinoma

Characteristic	Finding
Upper esophageal lesion (%)[a]	3.6
Midesophageal lesion (%)	39.8
Lower esophageal lesion (%)	56.6
Metastatic at diagnosis (%)	74.5
Associated squamous cell carcinoma (%)	23.2
Mean size of lesion (cm)	5.5

[a] Percent refers to the percentage of affected patients.

Table 2. Treatment Results

Treatment	No. of Patients	Mean Survival
None	8	13.1 days
Surgery	45	8 mo[a]
Chemotherapy	5	7.8 mo
Radiotherapy	8	4.1 mo
Surgery + chemotherapy	2	5.5 mo
Surgery + radiotherapy	1	4 mo
Surgery + chemotherapy + radiotherapy	1	6 mo
Chemotherapy + radiotherapy	1	9 mo
Dilatation	1	1 day

[a] This excludes 18% operative mortality.

Treatments and Prognosis

Mean overall survival for the 85 patients with evaluable survival data was 5.1 months. For the 64 patients who received some form of treatment, the mean survival was 5.6 months (Table 2). The results of surgical resection as the sole means of treatment were reported for 45 patients, 8 (18%) of whom died perioperatively. Of the 37 surgically treated patients who survived operation, mean survival was 8 months; all deaths were due to widespread metastatic disease. Three patients (8%) were alive at least 2 years after resection [10, 16]. Surgery with adjuvant chemotherapy or radiotherapy, or both, was reported in only 4 patients; survival ranged between 4 and 6 months.

Radiotherapy was the only treatment used in 8 patients with a mean survival of 4.1 months. Chemotherapy, using various drug combinations, was used alone in 5 patients with a mean survival of 7.8 months. One patient treated with a combination of CMC-VAP, ifosphamide, and VP-16 was free from disease at autopsy 11 months later; the patient died of unrelated causes [34]. Another patient survived 9 months after chemotherapy and was receiving radiotherapy for a local recurrence at the time of publication [22]. Chemotherapy appears to give striking clinical remission in most patients for varying lengths of time [17, 19, 26, 34, 35].

The small numbers of patients in each treatment group and the retrospective nature of this review preclude statistical comparisons between treatment groups. The much larger group of patients with pulmonary SCC does afford some historical precedents that may allow us to treat patients with esophageal SCC optimally.

Patients with pulmonary SCC have an approximate 2-year survival rate of 20% when treated with combination chemotherapy [46]. Pulmonary SCC patients also show improved survival when treated with chemotherapy after initial resection [47, 48]. In addition, newer data from several small series [49, 50] show an improved survival in pulmonary SCC patients treated with "salvage" or adjuvant surgical resection after an initial response to systemic chemotherapy. Although only about one third of patients initially treated with chemotherapy are candidates for surgical resection [46], these results are encouraging. The presence of residual tumor in 75% of resected specimens may provide justification for adjuvant surgical intervention [46, 49]. The use of postoperative chemotherapy and thoracic irradiation is also recommended if either nodal disease or residual tumor is present in the resected specimen [46, 51].

The use of prophylactic cranial irradiation in patients with pulmonary SCC is generally recommended because of the 60% to 80% incidence of central nervous system metastases [52, 53]. The incidence of central nervous system metastases in esophageal SCC patients is unknown, although they have been reported in several instances [9, 26, 35]. Careful evaluation of the central nervous system by neurological examination or radiological imaging should be considered in all patients with esophageal SCC and should be followed by cranial irradiation for affected patients [35].

Prospective randomized trials of therapy for esophageal SCC are unlikely given the rarity of the disease. We therefore recommend that patients with such a carcinoma be aggressively evaluated and managed by the surgeon, medical oncologist, and radiation oncologist using lessons learned from treatment protocols for pulmonary SCC. Systemic multidrug chemotherapy should be given either preoperatively or postoperatively, and consideration should be given to mediastinal and cranial irradiation if esophageal lymph nodes reveal metastatic disease.

Conclusion

Esophageal SCC is a rare but rapidly fatal malignancy if untreated. A review of the available data on 130 patients now reported in the literature revealed no optimal treatment protocols, although encouraging results of resection and intense chemotherapy in a few patients exist. Although less than ideal, lessons learned from the treatment of pulmonary SCC may need to be applied to patients with this unusual tumor. A recommendation for multiagent chemotherapy either in the preoperative or postoperative setting is warranted. Irradiation should also be used if mediastinal lymph nodes are involved or cranial metastases are present in an effort to salvage as many patients as possible from this lethal disease.

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Congenital Lesions of the Lungs

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CORRESPONDENCE

Extrinsic Obstruction of the Medtronic-Hall Disc Valve in the Mitral Position

To the Editor:

The recent report by Masters and Keon [1] on the extrinsic obstruction of a Medtronic-Hall disc valve in the mitral position should serve as a notice of caution to all cardiac surgeons who use prosthetic valves with tilting-disc occluders. Demonstrating the free movement of the tilting-disc occluder after prosthetic valve implantation in the native annulus does not insure against the problem of disc immobilization due to a prolapsing suture or the interposition of the cut end of the papillary muscle between the prosthetic valve ring and the disc once cardiac activity resumes. Also, the free movement of the disc occluder can be impaired by the contracting left ventricular myocardium [2], which is not apparent during the implantation of the prosthesis because of the cardioplegic relaxation of the left ventricular myocardium. This problem can be prevented by not selecting an oversized tilting-disc prosthetic valve.

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Mobilization Technique in Total Esophagectomy

To the Editor:

We read with interest the article by Inculet and co-workers [1] describing their technique for delivering the stomach or colon to the neck after total esophagectomy. We have been using Foley's catheter as a substitute to drains commonly used as described by Orringer [2–4] in transhiatal esophagectomy.

The stomach is transected at the cardia using an LS90G stapler (Ethicon Ltd). A stab gastrostomy is made in the dome of the gastric fundus, approximately 2 cm from the staple line. A Foley's catheter is introduced into the gastrostomy and the balloon is inflated with 5 to 7 mL of water. The distal valved end of the catheter is tied and sutured to the transected lower end of the esophagus. The intrathoracic esophagus is mobilized up and out of the cervical wound, thereby drawing the attached catheter through the posterior mediastinum. Gentle traction on this end of the catheter combined with guidance of the stomach through the widened diaphragmatic hiatus will bring the gastric fundus into the cervical wound. The balloon is then deflated and the catheter is withdrawn. The esophagogastric anastomosis can now be commenced in the usual manner after enlarging the gastrostomy stab wound. This method minimizes gastric trauma with the added advantage of avoiding possible axial rotation of the stomach during placement into the chest.

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Budd-Chiari Syndrome—Pathogenesis and Operative Repair

To the Editor:

The paper by Murphy and colleagues [1] perpetuates the confusion on the pathogenesis of inferior vena caval obstruction causing Budd-Chiari Syndrome. The essential pathological finding in their patient is described as a membranous web in the inferior vena cava (IVC) despite the obvious appearance of "hourglass" constriction of the IVC in the preoperative inferior vena cavogram and the need at operation to insert a pericardial patch graft. The pathology is essentially coarctation of the IVC, with obstruction being completed by folds of intima as in coarctation of the aorta [2–5].

The discussion does not describe procedures such as ventral cavoatrial bypass [6, 7], dorsal cavoatrial bypass [2–5, 8], dorsal cavo-caval venoplasty [9], and patch venoplasty [10–12], which have been used by other workers. We have performed a similar procedure using an inflow occlusion technique, in which the suprahepatic vena cava was occluded using a clamp, the intrahepatic IVC was occluded with a balloon, and the portal vessels were clamped at the porta hepatis [13]. Yu and Cheng [14] have applied a similar technique for direct open reconstructive surgery except that they cross-clamped the IVC above the renal veins and used 4°C heparinized Ringer's solution through the portal vein for continuous perfusion of the liver.

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Traumatic Rupture of Ascending Aorta and Left Main Bronchus

To the Editor:

I found the article by Sadow and associates [1] quite interesting. Their transpericardial approach for repair of the left mainstem bronchus is rather innovative. The indication for bronchoscopy in this case is quite clear. However, it is not clear from the article what prompted the thoracic aortography. Do the authors recommend aortography in all cases of mainstem bronchial disruption and/or sternal fracture? Was there some radiographic feature not mentioned in the article or discernible on the plain chest roentgenogram shown in the article that led to aortography? I would appreciate comments by the authors.

James C. Jones, MD

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Reference

1. Sadow SH, Murray CA III, Wilson RF, Mansoori S, Harrington SD. Traumatic rupture of ascending aorta and left main bronchus. Ann Thorac Surg 1988;45:682–3.

Reply

To the Editor:

The questions by Dr Jones are very pertinent. Rupture of a major bronchus has long been recognized to result in many instances from crushing, as it was in our patient, rather than deceleration [1]. In addition, force of impact studies on human cadavers using high-speed photography have shown that younger patients, such as ours (14 years old), showed virtually no skeletal damage from severe trauma, whereas older patients often showed multiple severe fractures [2]. In our patient, there were none of the changes on chest roentgenogram that usually make one suspect a traumatic rupture of the aorta. However, because of the apparent magnitude of the force required to rupture the mainstem bronchus and fracture the sternum, there was a high index of suspicion for a coexistent traumatic rupture of the aorta. Accordingly, even though a computed tomographic scan of the aorta was considered normal, an aortogram was requested. This showed a fairly typical traumatic rupture of the aorta distal to the left subclavian artery. Thus, in this and many other instances of traumatic rupture of the aorta, it is not any specific chest roentgenographic finding that is important, but rather the magnitude of force involved that should make one suspicious. Consequently, an isolated fracture of the sternum in an older patient by itself would not cause us to order an aortogram. This case also indicates that computed tomographic scans for diagnosing traumatic rupture of the aorta are not 100% accurate.

Robert F. Wilson, MD

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1. Peters RM, Loring WE, Sprunt WH. Traumatic rupture of the bronchus—A clinical and experimental study. Ann Surg 1958; 148:871–84.
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Treatment of Impending Sudden Cardiac Death

To the Editor:

My colleagues and I are pleased with the interest and discussion stimulated by our article [1]. I would, however, like to respond to the editorial [2] by Dr G. F. O. Tyers.

We did not then, nor do we now, recommend "routine implantation of the AICD [automatic implantable cardioverter defibrillator] with all revascularization procedures in patients with medically refractory ventricular arrhythmias." It is important to point out that our patients suffered, not simple ventricular arrhythmias, but multiple cardiac arrests. The average number of arrests per patient was 3.5. They all were refractory to numerous medications and most had easily inducible ventricular tachycardia or ventricular fibrillation. Our article reported the 2-year survival of such a population using combined revascularization and the AICD.

All patients, of course, met the criteria for AICD implantation that were established in 1980 [3] and are accepted by most groups worldwide using the device. In addition, all had severe coronary heart disease. With such an approach, we had an out of hospital resuscitation rate of approximately 35%, which we considered highly significant. These recurrences were clearly not predictable by postoperative electrophysiological data. We obviously are aware of false firings, and these are excluded from our data. The overall 2-year survival for such a high-risk group was 91%.

The proper place for considerations of cost effectiveness is difficult to assess in these patients with unpredictable cardiac arrest and indeed warrants further study and attention.

More selective use is clearly our ultimate goal as indicated in the last sentence of our paper. This will come as predictive data from electrophysiological studies improves. For the moment, when confronted with a patient population such as ours, with multiple cardiac arrests, especially secondary to ventricular fibrillation, we continue to believe that long-term survival in this group is best achieved with a combined approach.

Levi Watkins, Jr, MD

Associate Professor of Cardiac Surgery
Department of Surgery
The Johns Hopkins Hospital
600 N Wolfe St
Baltimore, MD 21205

References

1. Fonger JD, Guarnieri T, Griffith LSC, et al. Impending sudden cardiac death: treatment with myocardial revascularization and the automatic implantable cardioverter defibrillator. Ann Thorac Surg 1988;46:13–9.
2. Tyers GFO. Impending sudden death: treatment with myocardial revascularization and the automatic implantable cardioverter defibrillator [Editorial]. Ann Thorac Surg 1988;46:1–2.
3. Mirowski M, Reid PR, et al. Termination of malignant ventricular arrhythmias with an implanted automatic defibrillator in human beings. N Engl J Med 1980;303:322.

Reply

To the Editor:

Dr Watkins states "we did not . . . recommend routine implantation of the AICD with all revascularization procedures in patients with medically refractory ventricular arrhythmias." The key word is *refractory*, as he goes on to describe his population of treated patients as usually having inducible ventricular tachycardia or ventricular fibrillation and an average of 3.5 previous cardiac arrests. This patient group certainly falls within my understanding of refractory ventricular dysrhythmias. Further, I do not see any relevance to his reference to simple ventricular arrhythmias, as there is no suggestion in my editorial [1] that the AICD was used under those circumstances.

Dr Watkins is encouraged that 35% of his study patients had out of hospital activation of the defibrillator over the subsequent year or two after combined myocardial revascularization and AICD implantation. Most of this subset of patients was undoubtedly "rescued," but the extra hospitalization cost per treated patient, over requirements for myocardial revascularization alone, is $150,000. This is approximately three times more expensive than transplantation. The cost was so high because of the two additional asymptomatic patients who were exposed to the risks, complications, and expense of AICD implantation [2, 3] for each individual treated. Further, without constant out of hospital Holter or telemetry monitoring, how can Dr Watkins be absolutely certain that false firings were excluded from their data [3]?

All of the patients treated by Dr Watkins had met the criteria for AICD implantation, but that was before revascularization. I suspect that as many as half of them might not have fulfilled the criteria after the bypass operation, and the addition of sequential ablation procedures, even in the absence of ventricular aneurysm, might have benefited an additional group. Even poor ventricular function becomes a less distinct marker for early mortality after completion of a successful revascularization operation.

Dr Watkins and his associates are pioneers in the field of implantable defibrillators and they have achieved commendable results in the high-risk group of patients with ischemic heart disease and complex ventricular arrhythmias. However, until the technical refinements and improvements in longevity and reliability discussed in my editorial [1] are achieved, I must stand by my previous recommendations.

G. Frank O. Tyers, MD, FRCS (C)

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References

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2. Singer I, Hutchins GM, Mirowski M, et al. Pathologic findings related to the lead system and repeated defibrillations in patients with the automatic implantable cardioverter/defibrillator. J Am Coll Cardiol 1987;10:382–8.
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Complication of Aortic Dissection

To the Editor:

Reitknecht and colleagues [1] have reported a case of circumferential dissection of the ascending aorta extending beyond the aortic arch and intussusception of the intima of the ascending aorta and arch into the descending aorta. We concur with their management of this interesting case, as is evident in our earlier report [2]. However, we regret that we have to disagree with their statement "Our patient represents the second report in the literature [of this condition]." In fact, a few other cases [3, 4], in addition to ours, have been reported.

Panagiotis N. Symbas, MD

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References

1. Reitknecht FL, Bhayana JN, Lajos TZ. Circumferential intimal tear causing obstruction of the aortic arch: an unusual complication of aortic dissection. Ann Thorac Surg 1988;46:100–1.
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Tunneling of Defibrillator Leads

To the Editor:

With the establishment of the clinical efficacy and safety of the automatic implantable cardioverter defibrillator for the management of malignant ventricular arrhythmias [1, 2], an ever-increasing number of patients are undergoing implantation of this device. Regardless of the technique of implantation, the leads have to be tunneled from the site of implantation to the generator pocket. We have been using a simple technique for this purpose that eliminates the hazard of damage to the leads.

For primary automatic implantable cardioverter defibrillator implantation we use a left anterior thoracotomy incision. A Penrose drain is passed from the thoracotomy incision into the subcutaneous generator pocket. The ends of the leads are placed in this Penrose drain in a staggered fashion as shown in Figure 1. The drain is pulled into the pocket by applying gentle, steady traction.

We have used this technique in more than 90 patients with no instances of lead damage. This technique is simple and has been used for pacemaker procedures in the past. Its application for automatic implantable cardioverter defibrillator systems warrants reemphasis.

G. Hossein Almassi, MD
Gordon N. Olinger, MD

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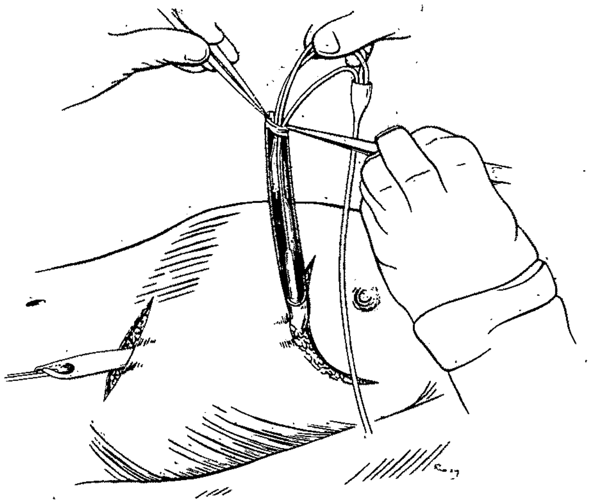

Fig. 1. The ends of the leads are introduced into the Penrose drain in a staggered fashion. The drain is then pulled into the pocket.

References

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Southern Thoracic Surgical Association Rules for Submission of Abstracts

Abstracts for papers to be presented for the 1989 Annual Meeting are now being accepted. The deadline for postmark of abstracts is May 15, 1989. An original and 1 copy should be submitted, using the official Association abstract form, to Bradley M. Rodgers, MD, Chairman, Program Committee, The Southern Thoracic Surgical Association, 111 E Wacker Dr, Chicago, IL 60601. Additional forms are available upon request from the Association.

Abstracts must summarize an original contribution not presented or accepted for presentation elsewhere. *Abstracts received after the deadline will not be considered.* The information requested at the bottom of this form must be completed indicating who is to receive the notice of acceptance or rejection and who will present the paper if accepted.

Abstracts may be submitted for the regular program, the Forum, or either. Papers selected for the Forum will be published in *The Annals of Thoracic Surgery* if they pass the usual editorial review.

Essayists are reminded that all papers accepted for presentation must be submitted in triplicate to Gordon F. Murray, MD, Secretary-Treasurer, at the time of presentation or to the Editor of *The Annals of Thoracic Surgery* prior to presentation.

Abstracts frequently obscure the value of their content because they are poorly organized. It is important that methods and results be clearly defined in the abstract; general statements such as "results will be presented" are not acceptable. When a procedure or method is stated to have "advantages," those advantages should be defined. Abstracts that simply summarize results without defining objectives and methods are equally undesirable.

Presentations in the regular program are limited to 10 minutes; those in the Forum are limited to 5 minutes.

In discussion of papers, the Association encourages a healthy spirit of constructive critical review and rebuttal by comments pertinent to the content of the paper being presented. Presentation of the discussion in the form of "secondary papers" will not be welcomed.

INSTRUCTIONS FOR ABSTRACTS

The official abstract form or photocopies must be used. **Authors must indicate whether they want the abstract considered for the regular program, the Forum, or either by checking the appropriate box. Authors must also categorize the principal subject of their abstract by checking the appropriate box.**

1. Title of abstract must be completely CAPITALIZED.
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I acknowledge that the material will not be presented elsewhere if accepted for presentation on the Southern Thoracic Surgical Association Scientific Program. I further understand that the editorial board of *The Annals of Thoracic Surgery* has the right of first refusal for publication of this material.

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EVENTS OF INTEREST

Brief notices of meetings, courses, and symposia relevant to cardiothoracic surgery are published as a service. They should be formatted as follows: meeting title, date, place, sponsor, accreditation, director, fee, minimum/maximum attendance, and address/phone for further information.

Announcements should be sent at least 4 months in advance of publication to *The Annals of Thoracic Surgery,* 3108 Queeny Tower, Barnes Hospital Plaza, St. Louis, MO 63110-1041; telephone, (314) 361-6084.

Transplantation for End-Stage Lung Disease: First International Seminar, Paris, France—April 8–9, 1989

This meeting is sponsored by The Autosuture Co, the Cystic Fibrosis Foundation, Sandoz Pharmaceuticals, and the Olympus Corporation. For information on this meeting, contact Beverly Farrier, Symposia Manager, ProMedica International, Inc, 620 Newport Center Drive, Suite 575, Newport Beach, CA 92660; or telephone (714) 640-5870.

Fundamentals of Cardiac Pacing, Bethesda, Maryland—April 10, 1989

Cardiac Pacing—1989, Bethesda, Maryland—April 11–13, 1989

Electrical Management of Tachyarrhythmias, Bethesda, Maryland—April 14, 1989

For information about these meetings, contact the American College of Cardiology, Learning Center, 9111 Old Georgetown Road, Bethesda, MD 20814; or telephone 1-800-253-4636, extension 241.

International Society for Heart Transplantation, Munich, Federal Republic of Germany—April 23–25, 1989

For information on this meeting, contact the Headquarters Office, 435 North Michigan Ave, Suite 1717, Chicago, IL 60611; or telephone (312) 644-0828.

Second International Symposium on Echocardiography and Doppler in Cardiac Surgery, Salzburg, Austria—May 1–3, 1989

For information on this meeting, contact G. Maurer, MD, or W. Mohl, MD, PhD, c/o Interconvention, A-1450 Vienna, Austria; or telephone 43-1-2369-2641 (telex, 11-18-03; facsimile, 43-1-2369-648).

Tenth Annual Scientific Session of the North American Society of Pacing and Electrophysiology, Toronto, Ontario, Canada—May 4–6, 1989

This meeting is accredited for credit hours in category 1 of the Physician's Recognition Award of the AMA, and application has been made to the Massachusetts Nurses Association for approval of contact hours. For information on this meeting, contact NASPE Registration, 13 Eaton Court, Wellesley Hills, MA 02181; or telephone (617) 237-1866.

Sixty-ninth Annual Meeting of The American Association for Thoracic Surgery, Boston, Massachusetts—May 8–10, 1989

For information on this meeting, contact AATS, 13 Elm St, Manchester, MA 01944; or telephone (508) 526-8330.

Vascular Surgery 1989, New York, New York—May 18–20, 1989

This symposium is cosponsored by the Long Island Vascular Clinic; the Long Island Jewish Medical Center; and the Postgraduate Institute for Medical and Dental Education, the Health Sciences Center, and the School of Medicine, State University of New York at Stony Brook. The symposium is accredited for 24 hours in category 1 from the Accreditation Council for Continuing Medical Education and the AMA. For information, contact Ann J. Boehme, CMP, Associate Director for Continuing Education, Long Island Jewish Medical Center, New Hyde Park, NY 11042; or telephone (718) 470-8650.

First International Symposium on Heart Failure: Mechanisms and Management, Jerusalem, Israel—May 21–25, 1989

This meeting is sponsored by the Israel Heart Society. For information, contact the Secretariat, First International Symposium on Heart Failure, PO Box 50006, Tel Aviv 61500, Israel; or telephone (03) 654571 (telex: 341171 KENS IL; facsimile; 972-3-655674).

Heart Surgery 1989: Third International Symposium on Cardiac Surgery, Rome, Italy—May 29–June 2, 1989

For information on this meeting, contact the Organizing Secretariat, Assistenza Internazionale Servizi di Congresso, Viale Parioli 2, Rome 00197, Italy.

General Thoracic Surgery, Toronto, Canada—June 1–2, 1989

For information on this meeting, contact Continuing Education, Faculty of Medicine, Medical Sciences Building, University of Toronto, Toronto, Ontario, M5S 1A8, Canada; or telephone (416) 978-2718.

Eighteenth Annual Society of Critical Care Medicine Educational and Scientific Symposium, New Orleans, Louisiana—June 5–9, 1989

For information on this meeting, contact the Society of Critical Care Medicine, 251 East Imperial Highway, Suite 480, Fullerton, CA 92635; or call (714) 870-5243.

First International Workshop on Cardiomyoplasty, Paris, France—June 6–8, 1989

This meeting is sponsored by Medtronic. For information on this meeting, contact Convergences, 16 Rue Jean-Jacques Rousseau, F 75001 Paris, France; or telex 216911 F (facsimile, 33-1-40130231).

International Symposium on Surgery for Heart Valve Disease, London, United Kingdom—June 12–16, 1989

This symposium is sponsored by Baxter Edwards CVS Division, Carbomedics, Medtronic, Pergamon Press, Inc, Shiley, St. Jude, and USCI International, and will focus on material and designs of replacement heart valves. The symposium is accredited for up to 30 hours of category 1 of the Physician's Recognition Award of the AMA. For information, contact the Symposium Secretariat, Conference Associates HVD, Congress House, 55 New Cavendish St, London W1M 7RE, United Kingdom; or telephone 01-486-0531 (telex: 934346 CONFAS G; facsimile: 01-935-7559).

International Society for Cardiovascular Surgery/Society of Vascular Surgeons, New York, New York—June 18–21, 1989

For information on this meeeting, contact the Association offices, 13 Elm St, Manchester, MA 01944; or telephone (508) 526-8330.

Western Thoracic Surgical Association, Monterey, California—June 21–25, 1989

For information on this meeting, contact the Association offices, 13 Elm St, Manchester, MA 01944; or telephone (508) 526-8330.

Surgery of the Airways, Boston, Massachusetts—July 17–18, 1989

This course is sponsored by the General Thoracic Surgical Department of the Massachusetts General Hospital and the Harvard Medical School Department of Continuing Education. The course is accredited for 16 hours in category 1 of the Physician's Recognition Award of the AMA. For information contact Harvard Medical School Department of Continuing Education, PO Box 825, Boston, MA 02117; or telephone (617) 732-1525.

Nineteenth World Congress of The International Society for Cardiovascular Surgery, Toronto, Ontario, Canada—September 5–9, 1989

For information on this meeting, contact XIX World Congress, ISCVS, I.T.S., PO Box 825, Deerfield, IL 60015.

Twenty-fifth Annual Meeting of The Society of Thoracic Surgeons, Baltimore, Maryland—September 10–13, 1989

For information on this meeting, contact George C. Kaiser, MD, The Society of Thoracic Surgeons, 111 East Wacker Dr, Chicago, IL 60601-4301; or telephone (314) 644-6610.

Thirty-sixth Annual Meeting of the Southern Thoracic Surgical Association, Phoenix, Arizona—November 9–11, 1989

For information on this meeting, contact Gordon F. Murray, MD, Southern Thoracic Surgical Association, 111 East Wacker Dr, Chicago, IL 60601-4301; or telephone (314) 644-6610.

Seventh Congress of the European Society of Biomechanics, Aarhus, Denmark—July 8–11, 1990

For information on this meeting, contact Seventh Congress of ESB, Biomechanics Laboratory, Orthopaedic Hospital, Randersvej 1, 8200 Aarhus N, Denmark; or telephone 45-616-7500, extension 4649.

Classified ads for positions wanted or available must relate only to the thoracic or cardiovascular surgical specialties. Display space (minimum, ¼ page) is also available through Media for Medicine, Inc, 130 Madison Avenue, New York, NY. All ads are subject to the approval of the editor, and material deemed inappropriate for publication in *The Annals* will be rejected. If anonymity is desired, please indicate this at the time of submission and a code number will be assigned. All responses received will remain confidential in the publisher's office and will be conveyed to the advertiser shortly after receipt. The charge for all classified advertising is **$1.10 per word per insertion, minimum 20 words. There is an additional fee of $13.00 per insertion for box number ads.** The copy deadline is 7 weeks prior to publication, eg, for the March issue, copy should be received by the 1st of January. Ad copy should be typed double-spaced and mailed in duplicate to: *The Annals of Thoracic Surgery*, Desk Editorial, Classified Ads, Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010. Make *nonrefundable* check payable to Elsevier Science Publishing Co, Inc.

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Thoracic-vascular surgeon, board certified, wanted for suburban Massachusetts, noncardiac thoracic and some vascular practice. Initial response should include curriculum vitae, clinical experience, and names of references.

Please respond to A-892, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiovascular and thoracic surgeon: Excellent opportunity for a board certified/eligible cardiovascular and thoracic surgeon to join very busy southern California 6-man group. Practice specializing in adult and pediatric thoracic and cardiovascular surgery. Experience in heart transplantation desirable. Excellent benefit package. Please reply with curriculum vitae.

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Cardiac surgeon seeking associate in active cardiac program (95% cardiac—5% general thoracic—no vascular). 500-bed tertiary-care hospital in Midwest with general surgery residency training program. Must be board eligible and obtain board certification within 3 years. Salary leading to partnership. Send CV and recent photograph.

Please respond to A-908, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiovascular and thoracic surgeon experienced in cardiac surgery as well as general thoracic surgery needed to join the practice of an established thoracic and cardiovascular surgeon in the Los Angeles County/South Bay area. Send curriculum vitae and details of experience.

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Cardiothoracic and vascular surgeon, BE/BC, wanted to join expanding 2-man private practice in South Jersey. Please send curriculum vitae and photograph. Recent graduate preferred.

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Cardiothoracic/vascular surgeon: B/C in general and thoracic surgery. Minimum two years of practice experience. Very active private three-surgeon practice. Located in western Pennsylvania. Salary leading to full partnership. Excellent benefits. Detailed CV must accompany response. All replies treated confidentially.

Please respond to A-107, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiothoracic surgeon, BE/BC, wanted to join surgeon in active cardiac/thoracic/vascular surgical practice in northern Alabama community of 80,000 (300,000 population draw). Clinical practice in two community hospitals. Lake/mountain recreation facilities. Generous compensation, future partnership.

Please write: Sara Fleming, Business Manager, 206 Bay St, Gadsden, AL 35901; telephone (205) 543-7501.

Cardiothoracic surgeon, BC/BE, recent graduate, to join 3-man group for private practice in 500-bed teaching hospital, Great Lakes area, currently active in cardiac procedures. Practice includes open heart, thoracic, and vascular and pacemaker cases. Replies kept confidential. Send CV, list of cases, and references.

Please respond to A-108, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiovascular surgeon wanted to join a 2-man group in an established practice in the Southeast. Would prefer a recent graduate, but all applications considered. Generous salary leading to partnership. Practice includes all aspects of adult cardiac, thoracic, and vascular surgery. Send curriculum vitae with experience, recommendations, and photograph.

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Cardiothoracic surgeon needed for rapidly expanding program located in a coastal area of the Southeast. Private practice, primarily adult cardiac and thoracic. BC/BE required. Respond with curriculum vitae, photograph, and names of references.

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Faculty position: The Division of Thoracic and Cardiovascular Surgery, Southwestern Medical School of the University of Texas Southwestern Medical Center, is seeking an individual with strong clinical background in adult cardiovascular/thoracic surgery, along with a commitment to education and research, for a position at the assistant professor level. Must be ABTS certified or eligible.

Send complete curriculum vitae to W. Steves Ring, MD, Chairman, Division of Thoracic and Cardiovascular Surgery, UT Southwestern Medical Center, 5323 Harry Hines Boulevard, Dallas, TX 75235-9031. An equal opportunity employer.

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For confidential consideration, please submit curriculum vitae to A-117, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiovascular thoracic surgeon to join a multisurgeon private practice in the Midwest. Must be board eligible or certified. Must have expertise and experience in all aspects of adult cardiac and thoracic surgery. Generous compensation/future partnership. Send curriculum vitae outlining surgical experience, training, and references.

Please respond to A-118, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

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Please respond to A-126, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Wanted: Assistant surgeon/house physician for cardiovascular and thoracic surgical service. Heart Center at St. Vincent Charity Hospital and Health Center.

Reply to: Cardio-Vascular Surgeons, Inc, 2322 E 22nd St, Suite 208, Cleveland, OH 44115-3176.

The Division of Thoracic and Cardiovascular Surgery, Department of Surgery, at the University of Maryland is seeking a cardiothoracic intensivist to work in a cardiac surgery ICU. The successful candidate must be board eligible/board certified in Surgery, Internal Medicine, or Anesthesiology with special eligibility or certification in Critical Care. Salary commensurate with experience. Experience in clinical research helpful.

Applicants should submit a current curriculum vitae and three professional references to Joseph S. McLaughlin, MD, Professor and Head, Thoracic and Cardiovascular Surgery, University of Maryland Professional Building, c/o Suite 320, 419 W Redwood St, Baltimore, MD 21201. AA/EOE.

Cardiothoracic surgeon, board certified with 2 to 4 years experience in cardiac surgery, wanted to join a growing group of cardiac surgeons, cardiologists, and pulmonologists in the Pacific Northwest. General thoracic and vascular experience necessary. Research opportunities available, academic links possible. Salary leading to full partnership in 2 or 3 years; potential exists for leadership in major cardiac program.

Please send curriculum vitae to John R. Bauman, Administrator at The Thoracic Clinic, PC, 507 NE 47th Ave, Portland, OR 97213-2282.

Thoracic-vascular surgeon: Board certified or eligible surgeon wanted to join very active noncardiac thoracic vascular practice in small community with referral base of approximately 125,000. Salary leading to full partnership. Advantages of living in a small community in eastern Ohio less than one hour from large desirable metropolitan area. Will also consider applicants primarily interested in vascular surgery. Respond with curriculum vitae.

Please respond to A-125, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiothoracic surgeon: The University of Maryland, Department of Surgery, is seeking a Cardiothoracic Surgeon at the Assistant Professor level, effective July 1, 1989. Successful candidates should have special expertise in pediatric cardiothoracic surgery and transplantation with a major commitment to an academic career effective July 1, 1989. Excellent University fringe benefits package and salary commensurate with experience.

Please send curriculum vitae and three professional references to Joseph S. McLaughlin, MD, Professor and Head, Division of Cardiovascular and Thoracic Surgery, Department of Surgery, University of Maryland Professional Building, Suite 320, 419 W Redwood St, Baltimore, MD 21201. AA/EOE.

The University of California, Irvine, Department of Surgery, Division of Thoracic Surgery, is offering a position at the fellowship level with a concurrent Clinical Instructor faculty position in cardiovascular laser surgery. The position is open to graduates of programs in cardiac and/or vascular surgery and includes research in laboratory and clinical applications of laser radiation to cardiovascular surgery. Board certification or eligibility required.

Reply with CV and list of references to G. Robert Mason, MD, Professor and Chairman, Department of Surgery, UCI Medical Center, 101 The City Drive, Orange, CA 92668 by April 1, 1989. The University of California is an affirmative action/equal opportunity employer.

The Department of Surgery, University of California, San Francisco, is seeking an academically oriented cardiothoracic surgeon, at the Assistant/Associate Professor level, for Chief of Cardiothoracic Surgery at the San Francisco Veteran's Administration Medical Center. Applicant must be board certified in cardiothoracic surgery and have independent operating experience in adult cardiac and general thoracic surgery, administrative experience, and background in cardiac surgical research and education. The candidate will be a full-time member of the Division of Cardiothoracic Surgery, Department of Surgery, University of California, San Francisco.

Interested individuals should submit curriculum vitae to Donald J. Magilligan, MD, Chief, Cardiothoracic Surgery, Room 896-M, University of California, San Francisco, CA 94143-0118. The University of California, San Francisco, is an equal opportunity/affirmative action employer. Women and minorities are encouraged to apply.

Heart transplant surgeon. Established 5-man thoracic and vascular surgery practice in medium-sized midwestern city seeks a surgeon capable of organizing and heading our transplant team. We currently do more than 600 open hearts annually and have just received provisional state approval for transplantation. The ideal candidate will also have the necessary training and experience to work in our established pediatric thoracic surgery program and do a limited number of adult open hearts while devoting the bulk of his time and energy to implementing the transplant project. Very attractive compensation package including guaranteed salary. Please send curriculum vitae.

Please respond to A-123, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiovascular and thoracic surgeon BC/BE wanted for established 3-man group in Northeastern Ohio. Adult cardiac, vascular, and thoracic experience needed. Please send curriculum vitae.

Please respond to A-124, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiothoracic and vascular surgeon, board eligible/certified with experience in adult cardiac thoracic and vascular surgery, wanted to join well established 2-surgeon practice located in South Florida. Send CV and photo.

Please respond to A-122, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiothoracic surgeon, board certified or eligible, needed to join a busy adult cardiac surgery practice. Opportunity to join two cardiac surgeons performing over 400 open heart procedures annually in a competitive environment in south central Pennsylvania.

Please respond with curriculum vitae, clinical experience, and references to Robert A. Albus, MD, 650 N Twelfth St, Lemoyne, PA 17043, or call (717) 763-7551.

Postresidency clinical associate position available in cardiopulmonary surgery with University-based large service starting July 1989 or January 1990 for 1 to 2 years. Up to 25% research opportunity option available. Complete training in cardiopulmonary surgery desirable. Must be a graduate of an American medical school and eligible for full licensure in Oregon.

Please respond to Albert Starr, MD, 9155 SW Barnes Rd, Suite 240, Portland, OR 97225.

Cardiothoracic surgeon to join established group in northwest Indiana (very near Chicago). Excellent salary. Please respond with curriculum vitae.

Please respond to A-121, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Faculty Position—The Division of Cardiopulmonary Surgery, Oregon Health Sciences University, is seeking two individuals with strong background in adult and pediatric cardiovascular surgery for position at the assistant professor level.

Send complete curriculum vitae to Albert Starr, MD, Professor and Chief, Cardiopulmonary Surgery, Oregon Health Sciences University, 3181 SW Sam Jackson Park Rd, Portland, OR 97201. Oregon Health Sciences University is an equal opportunity employer.

Cardiovascular and thoracic surgeon wanted for an established practice in Dallas, TX. Candidate must be board certified or eligible.

Please send curriculum vitae to Dallas Cardiovascular Surgery Associates, 7777 Forest Lane, Suite A-323, Dallas, TX 75230.

SITUATIONS WANTED

Cardiovascular and thoracic surgeon, 34, recent graduate, ABS certified, ABTS eligible. Additional year of experience in all aspects of cardiac surgery. Wishes to join an active cardiothoracic practice. Curriculum vitae, operative experience, and references available upon request.

Please respond to W-545, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Pediatric cardiac surgeon, university-trained with additional fellowship training in congenital heart surgery; seeking an academic position in cardiothoracic surgery with primary responsibility to infants and children. Experience with research and publication and interested in investigating neonatal myocardial ischemia, protection, and preservation; available July 1989.

Please respond to W-548, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiovascular and thoracic surgeon, 42, American, ABS, ABTS, ABVS. Eight years private practice experience. Completing overseas fellowship in heart and heart/lung transplantation July 1989. Seeks opportunity with program involved in transplant surgery. Curriculum vitae and references upon request.

Please respond to W-546, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiovascular and thoracic surgeon, mid-50's. University trained, ABS/ABTS, 14 years of extensive and highly successful solo practice in vein and IMA CABG, valve, pulmonary and vascular surgery. Experienced in starting open heart program. Strong surgical and clinical skills. Seeking private practice opportunity, either starting new program or in association with established individual or group.

Please respond to W-100, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiovascular and thoracic surgeon, 40, wishes to relocate, preferably in the Southeast. American university trained, ABS, ABTS, FACS. Private practice experience in adult cardiac, thoracic, and peripheral vascular surgery. Willing to initiate new program. Curriculum vitae and references upon request.

Please respond to W-101, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiac, vascular, and thoracic surgeon, 50, wishes to relocate. Academic background with numerous publications. Greater than 10 years private practice—set up open heart unit. CV on request.

Please respond to W-103, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiovascular and thoracic surgeon. 31 yr. ABS/BC. Will finish U Toronto CVT residency (ABTS/BE) July 1989. Excellent references. Seek stable private practice association with senior partner(s) in adult cardiac.

40 Baywood Ct, Thornhill, Ontario L3T 5W3 Canada; 416-889-4078.

Cardiothoracic surgeon, 33, ABS certified, ABTS eligible, available July 1989. University trained with experience in IMA grafts, coronary surgery, valvular surgery. Solid exposure to complex congenital surgery and electrophysiology. Seeks private practice situation but would be delighted to accept some academic responsibilities. Prefer Mid-to-North Atlantic states or Midwest.

Please respond to W-104, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Chief resident in cardiothoracic surgery in major New York training program, finishing June 1989. Interested in private practice in Northeast. Curriculum vitae and references upon request.

Please respond to W-105, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiovascular and thoracic surgeon wishes to relocate. University trained with ABTS certification. Ten years' experience with extensive cardiac, thoracic, and peripheral vascular surgery. Would be interested in starting new program or association with group. Curriculum vitae and references available upon request.

Please respond to W-110, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiothoracic surgeon, 42, seeks relocation to Chicago area. University trained, ABTS/ABS certified, STS, FACS. Nine years private practice in Ohio, extensive experience in adult cardiac surgery, including IMA, mitral valve repair, PTCA support. Active in teaching, 22 publications. Would consider private or academic position, willing to initiate new cardiac program. Curriculum vitae on request.

Please respond to W-107, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Pediatric and adult cardiovascular surgeon, 33, board eligible, seeking staff position. Extensive training in both complex congenital and adult valve and coronary surgery. Experienced in internal mammary artery grafting. Proficient in preoperative and postoperative management of adult and pediatric patients. Curriculum vitae and references on request.

Please respond to W-108, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiac surgeon, 35, foreign medical graduate. Extensive experience in both congenital and adult valve and coronary surgery. Two years of fellowship in major North American medical centers. Very strong academic background. Seeks opportunity with a university academic program or a private group. Available July 1989.

Please respond to W-106, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

Cardiovascular and thoracic surgeon looking for a position to first assist with busy cardiovascular surgeon or group. More than 10 years experience after training.

Please respond to W-109, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

FELLOWSHIPS

The Department of Surgery and Division of Cardiothoracic Surgery has immediate openings for Clinical Fellows in Adult and Pediatric Cardiothoracic Surgery.

Please respond to T. D. Ivey, MD, Division of Cardiothoracic Surgery, Department of Surgery, University Of Cincinnati Medical Center, 231 Bethesda Avenue, Cincinnati, OH 45267-0558.

Fellowship in thoracic and cardiovascular surgery available July 1989.

Contact Dr Harold C. Urschel, 3600 Gaston Avenue, Suite 1201, Dallas, TX 75246; telephone (214) 824-2503.

Fellowship in cardiovascular surgery for 1 year available January 1 or July 1 with group doing approximately 1,000 cardiac procedures per year and large volume of vascular procedures. ABS eligible or certified, California medical license required or readily obtainable. Ideal for a person between general surgery residency and thoracic surgery residency.

Please respond with curriculum vitae to Bradley J. Harlan, MD, 5301 F Street, Suite 312, Sacramento, CA 95819.

Surgical fellow: Clinical fellowship position available in adult and pediatric cardiothoracic surgery. Large volume of cases. NJ license required. Excellent salary and benefits.

Please contact Lorenzo Gonzalez-Lavin, MD, Dept of Surgery, Deborah Heart & Lung Center, Browns Mills, NJ 08015.

Research fellowship in thoracic oncology available for 2 to 3 years. Projects include the immunology and biology of lung cancer and studies on mechanisms of metastases. Salary is supported by an NIH Training Grant.

Send curriculum vitae and three references to Dr Jack A. Roth, Chairman, Department of Thoracic Surgery, Box 109, University of Texas MD Anderson Hospital and Tumor Institute, 1515 Holcombe Blvd, Houston, TX 77030. An equal opportunity/affirmative action employer.

Clinical fellowship in adult cardiothoracic surgery available. Excellent stipend and fringe benefits.

Please send curriculum vitae to Eldred D. Mundth, MD, Bryn Mawr Medical Building, North, 830 Old Lancaster Road, Bryn Mawr, PA 19010.

Cardiac surgery research fellowship: Research fellowship in cardiac surgery available for 1–2 years beginning in July 1989. Major projects include laboratory and clinical research in cardiomyoplasty, the use of skeletal muscle for cardiac assist. Position also provides access to leading thoracic surgery training program. Salary is negotiable.

Contact James D. Sink, MD, The Emory Clinic, Section of Cardio-thoracic Surgery, 1365 Clifton Road, NE, Atlanta, GA 30333; (404) 321-0111, Extension 3616.

Fellowship, thoracic surgical oncology: Position available July 1989 in the Department of Thoracic Surgery and Oncology at Roswell Park Memorial Institute, Buffalo, NY. Training will focus on diagnosis, treatment, and research in the intrathoracic malignancies, especially lung cancer. Areas of interest include surgery, chemotherapy, immunology, and immunotherapy. Applicants must have had at least 3 years of approved residency training in the US.

Interested candidates should contact H. Takita, MD, DSc, FACS, Chief, Department of Thoracic Surgery and Oncology, Roswell Park Memorial Institute, Elm and Carlton Streets, Buffalo, NY 14263; (716) 845-8574 or 845-2300. An equal opportunity/affirmative action employer.

Fellowship in cardiothoracic surgery for 1 year available July 1 in a university-affiliated program. Candidate must be ABS eligible or certified; Pennsylvania medical license required. Excellent salary and all expenses paid including malpractice insurance. Candidate *will be performing* all aspects of adult cardiothoracic and vascular surgery. Opportunities for research and teaching are available. This program is designed for the surgeon who is between a general surgery residency and a thoracic surgery residency.

Please respond with curriculum vitae to Arthur J. Roberts, MD, Director, The Heart Institute, Suite 340, 35 West Linden Street, Wilkes-Barre, PA 18702.

Senior Fellow in Thoracic and Cardiovascular Surgery at the Lahey Clinic Medical Center, Burlington, MA, available from July 1, 1990, to December 31, 1990. This position will involve all aspects of cardiothoracic surgery, with special emphasis on pulmonary and esophageal surgery. Opportunity for clinical research.

Address inquiries to David M. Shahian, MD, Chairman, Department of Thoracic and Cardiovascular Surgery, Lahey Clinic Medical Center, 41 Mall Rd, Burlington, MA 01805.

Fellowship in cardiothoracic surgery. Major New York City teaching hospital. July 1989 to June 1990, ABS/ABTS eligibility certification required. Competitive salary and benefits.

Please respond with curriculum vitae and reference letters to Randall B. Griepp, MD, Director, Division of Cardiothoracic Surgery, The Mount Sinai Hospital, 1 Gustave Levy Place, Box 1028, New York, NY 10029.

Fellowship in adult cardiac surgery available July 1 for 1 or 2 years in private program performing over 600 open heart procedures yearly. Full general surgery training required. ECFMG and visa-qualified foreign applicants accepted.

Send curriculum vitae to Donald R. Kahn, MD, 817 Princeton Ave, Suite 300, Birmingham, AL 35211.

CARDIOVASCULAR AND THORACIC SURGEON, Board certified or eligible, wanted to join established private practice in Ft. Lauderdale, Florida.

Please send curriculum vitae, photo, and clinical experience.

Please respond to:

Chalit Cheanvechai, M.D.
PO Box 11620
Ft. Lauderdale, Florida 33339

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FELLOWSHIP IN THORACIC SURGERY

The Surgery Branch of the National Cancer Institute, National Institutes of Health has an immediate opening for a Fellowship in Thoracic Surgery. This program offers a broad experience in thoracic oncologic surgery with opportunities to participate in clinical and basic research. A two-year program is available for candidates desiring additional research experience. Applicants must be Board Eligible in Thoracic Surgery. Please submit a current curriculum vitae and bibliography. Salary for this Fellowship position is dependent on background and qualifications.

CONTACT:
Harvey T. Pass, M.D.
Head, Thoracic Oncology Section
Surgery Branch
National Cancer Institute
Bldg. 10, Room 2B07
9000 Rockville Pike
Bethesda, Maryland 20892
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At CryoLife,® we know that the future durability and longevity of cryopreserved allograft heart valves is directly related to valve leaflet cell viability at the time of implant. Proper cell preservation techniques assure that normal tissue tensile strength is maintained over the lifetime of the allograft. This relationship between allograft durability and cell viability is supported by the 12 year O'Brien clinical study on allograft valves, *Journal of Thoracic and Cardiovascular Surgery,* December 1987.

Since September 1984, CryoLife has spent in excess of one million dollars on research and development of advanced cell preservation techniques at 17 U.S. universities and clinics. Our patent pending cryopreservation process assures at least 75% (x 88.5 ± 12.27%) cell viability of human heart valve leaflet fibroblasts. Over this 46 month clinical experience, we have preserved over 5,669 human valves, of which 3,600 have been implanted. To date, only 11 post-operative valve-related complications have been reported — a .003% cumulative failure ratio.

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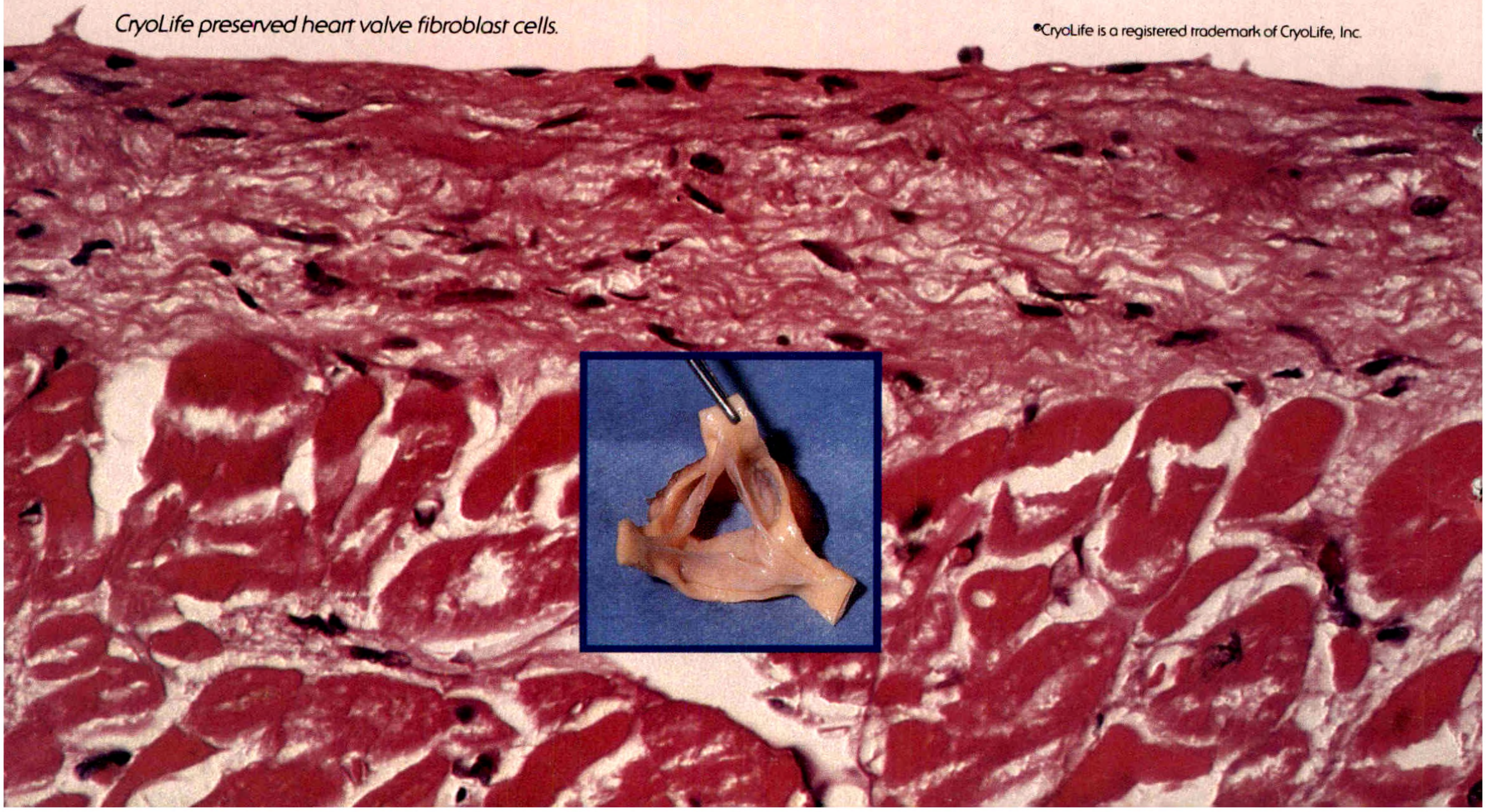
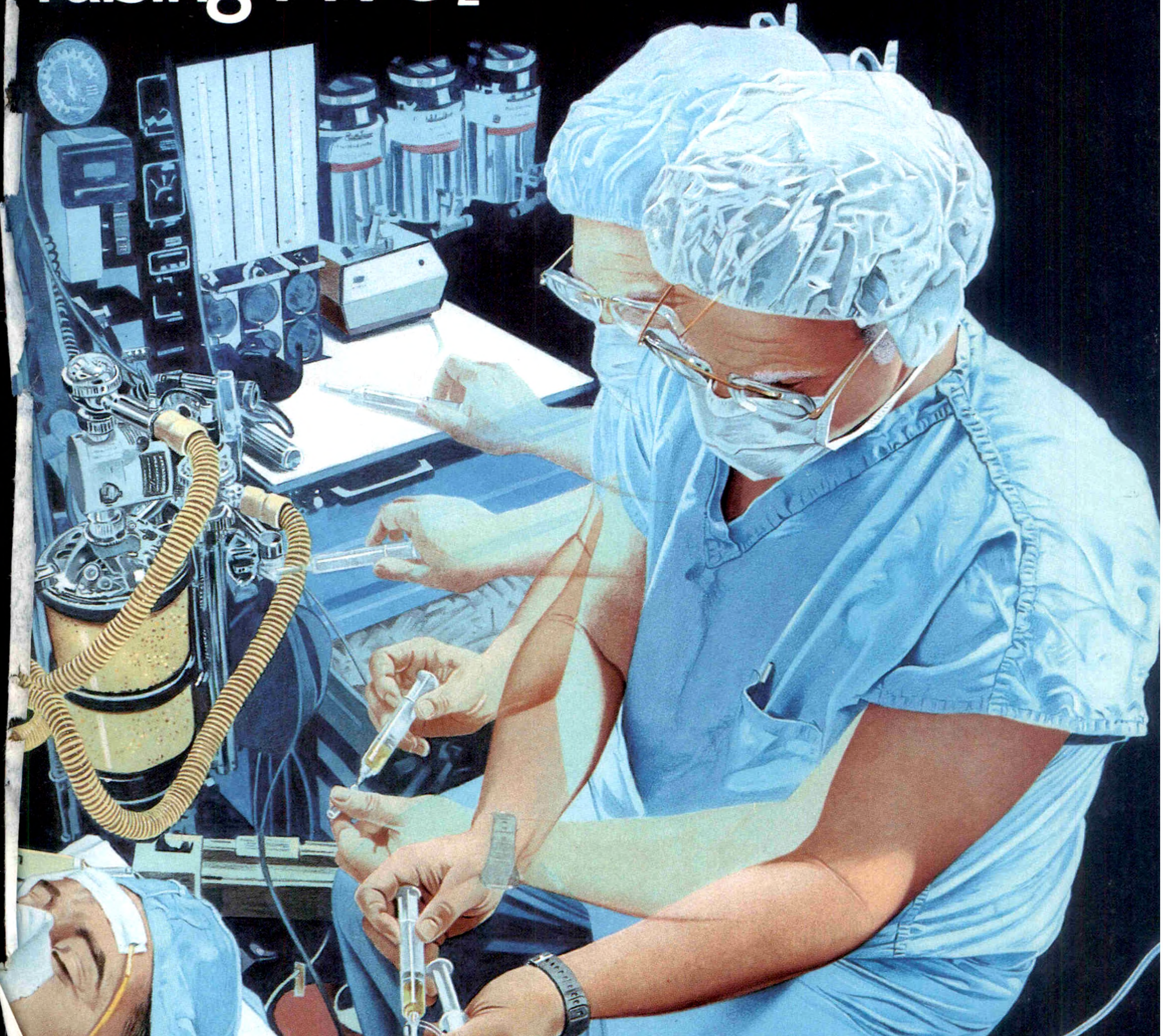


CryoLife preserved heart valve fibroblast cells.

Compromised output, ischemia, and the highly vulnerable cardiac surgery patient...

The next crucial step: raising output without raising MVO_2



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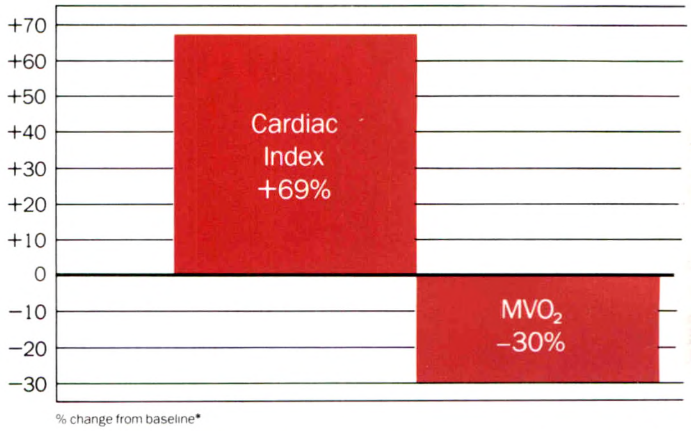
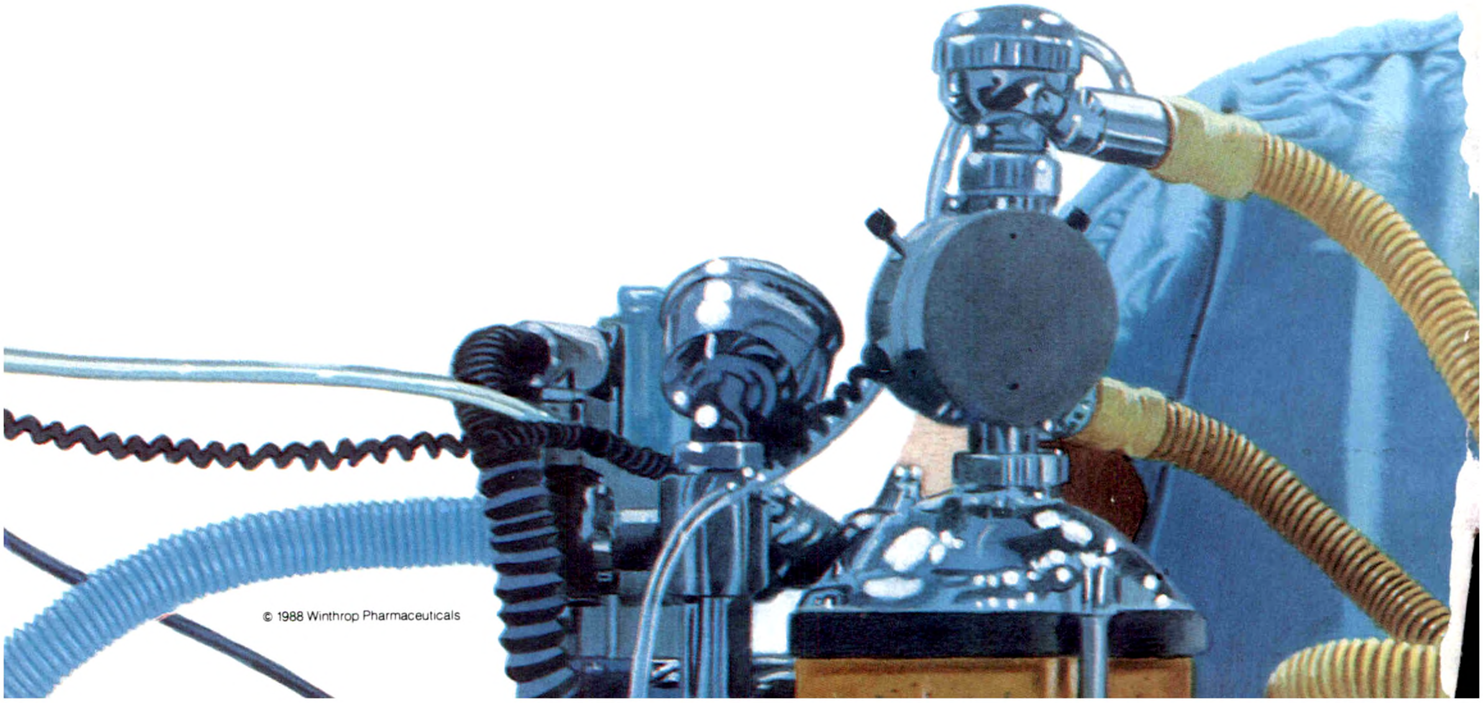
INOCOR I.V. (amrinone) provides improved hemodynamics without raising MVO_2 and worsening myocardial ischemia[1]



*n=8. Adapted from Benotti et al.[1] Amrinone was infused in patients with severe congestiv
failure due to coronary artery disease at 2.5 mg/kg over 1 hour.

1. Benotti JR, Grossman W, Braunwald E, et al: Effects of amrinone on myocardial energy metabolism and hemodynamics in patients with severe congestive heart failure due to co artery disease. *Circulation* 1980;62:28–34.
2. Baim DS: Effects of amrinone on myocardial energetics in severe congestive heart fail *Am J Cardiol* 1985;56:16B–18B.

"…hemodynamic improvements with catecholamine agents such as dobutamine tend to be achieved only at the expense of a 30 to 40% increase in myocardial oxygen…."[2]



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- Unique mechanism of action—PDE III inhibition
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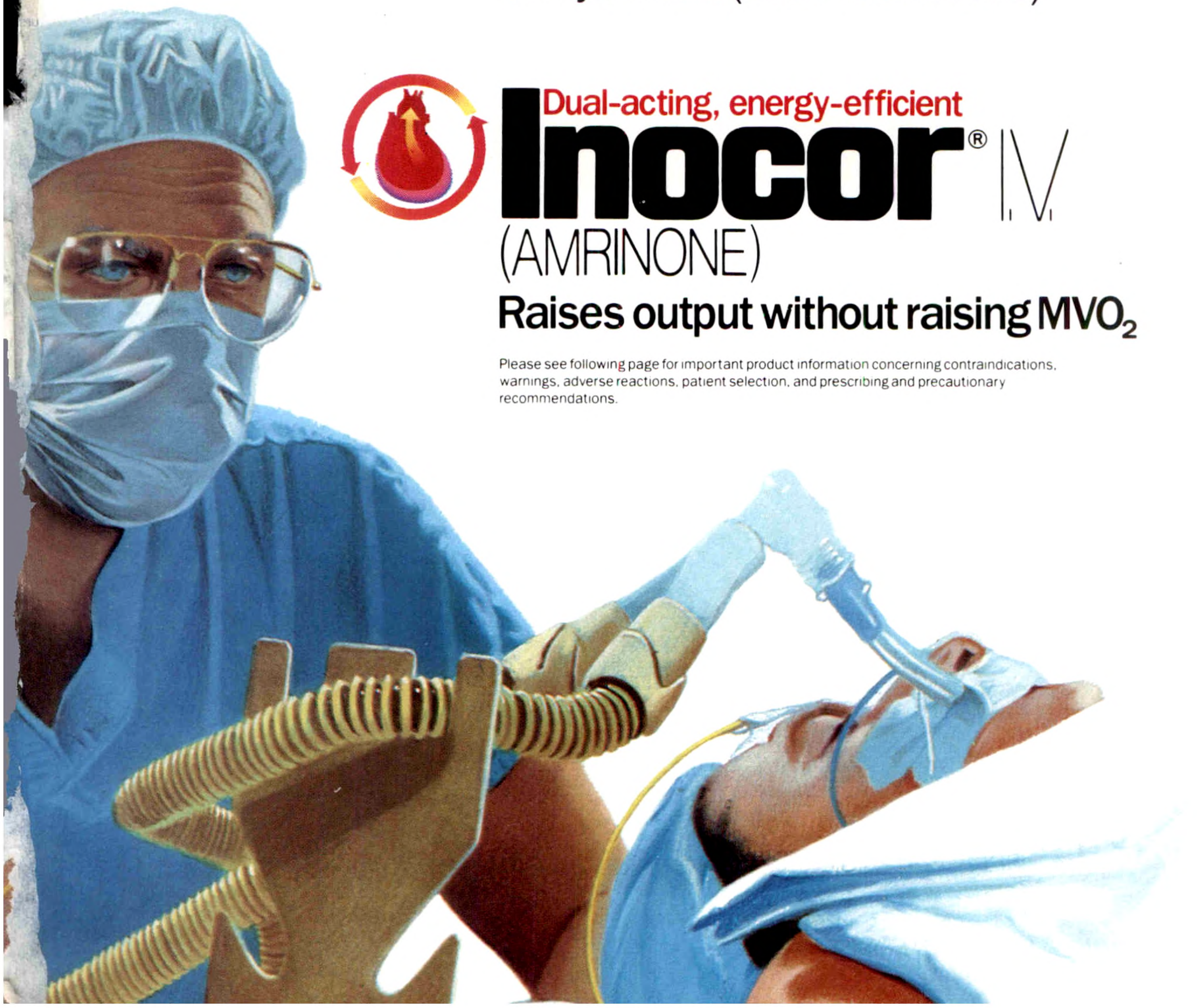
(AMRINONE)

Raises output without raising MVO_2

Please see following page for important product information concerning contraindications, warnings, adverse reactions, patient selection, and prescribing and precautionary recommendations.



INOCOR I.V.: Potent inotropic action in low output syndrome without increasing MVO_2 or aggravating myocardial ischemia

- A unique mode of action—selective PDE III inhibition
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- No significant increase in risk of arrhythmias (see Precautions)
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- Unlike catecholamines, does not act on the beta receptors—may be used effectively in patients on beta blockers

Brief Summary

Please consult full product information before prescribing. A summary follows.

INOCOR lactate injection, brand of amrinone lactate, represents a new class of cardiac inotropic agents with vasodilator activity, distinct from digitalis glycosides or catecholamines.

INDICATIONS AND USAGE INOCOR lactate injection is indicated for the short-term management of congestive heart failure. Because of limited experience and potential for serious adverse effects (see ADVERSE REACTIONS), INOCOR should be used only in patients who can be closely monitored and who have not responded adequately to digitalis, diuretics, and/or vasodilators. Although most patients have been studied hemodynamically for periods only up to 24 hours, some patients were studied for longer periods and demonstrated consistent hemodynamic and clinical effects. The duration of therapy should depend on patient responsiveness.

CONTRAINDICATIONS INOCOR lactate injection is contraindicated in patients who are hypersensitive to it. It is also contraindicated in those patients known to be hypersensitive to bisulfites.

PRECAUTIONS *General:* INOCOR lactate injection should not be used in patients with severe aortic or pulmonic valvular disease in lieu of surgical relief of the obstruction. Like other inotropic agents, it may aggravate outflow tract obstruction in hypertrophic subaortic stenosis.

During intravenous therapy with INOCOR lactate injection, blood pressure and heart rate should be monitored and the rate of infusion slowed or stopped in patients showing excessive decreases in blood pressure.

Patients who have received vigorous diuretic therapy may have insufficient cardiac filling pressure to respond adequately to INOCOR lactate injection, in which case cautious liberalization of fluid and electrolyte intake may be indicated.

Supraventricular and ventricular arrhythmias have been observed in the very high-risk population treated. While amrinone per se has not been shown to be arrhythmogenic, the potential for arrhythmia, present in congestive heart failure itself, may be increased by any drug or combination of drugs.

Thrombocytopenia and hepatotoxicity have been noted (see ADVERSE REACTIONS).

INOCOR is not recommended for use in acute myocardial infarction.

LABORATORY TESTS *Fluid and electrolytes:* Fluid and electrolyte changes and renal function should be carefully monitored during amrinone lactate therapy. Improvement in cardiac output with resultant diuresis may necessitate a reduction in the dose of diuretic. Potassium loss due to excessive diuresis may predispose digitalized patients to arrhythmias. Therefore, hypokalemia should be corrected by potassium supplementation in advance of or during amrinone use.

DRUG INTERACTIONS In a relatively limited experience, no untoward clinical manifestations have been observed in patients in whom INOCOR lactate injection was used concurrently with the following drugs: digitalis glycosides; lidocaine, quinidine; metoprolol, propranolol; hydralazine, prazosin; isosorbide dinitrate, nitroglycerine; chlorthalidone, ethacrynic acid, furosemide, hydrochlorothiazide, spironolactone; captopril; heparin, warfarin; potassium supplements; insulin; diazepam.

One case of excessive hypotension was reported when amrinone was used concurrently with disopyramide.

Until additional experience is available, concurrent administration with Norpace® (disopyramide) should be undertaken with caution.

CHEMICAL INTERACTIONS A chemical interaction occurs slowly over a 24-hour period when the intravenous solution of INOCOR lactate injection is mixed directly with dextrose (glucose)-containing solutions. **THEREFORE, INOCOR LACTATE INJECTION SHOULD NOT BE DILUTED WITH SOLUTIONS THAT CONTAIN DEXTROSE (GLUCOSE) PRIOR TO INJECTION.**

A chemical interaction occurs immediately, which is evidenced by the formation of a precipitate when furosemide is injected into an intravenous line of an infusion of amrinone. Therefore, furosemide should not be administered in intravenous lines containing amrinone.

USE IN PREGNANCY *Pregnancy category C:* There are no adequate and well-controlled studies in pregnant women. Amrinone should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

USE IN NURSING MOTHERS Caution should be exercised when amrinone is administered to nursing women, since it is not known whether it is excreted in human milk.

USE IN CHILDREN Safety and effectiveness in children have not been established.

ADVERSE REACTIONS *Thrombocytopenia:* Intravenous INOCOR lactate injection resulted in platelet count reductions to below $100,000/mm^3$ or normal limits in 2.4% of patients.

Gastrointestinal effects: Gastrointestinal adverse reactions reported with INOCOR lactate injection during clinical use included nausea (1.7%), vomiting (0.9%), abdominal pain (0.4%), and anorexia (0.4%).

Cardiovascular effects: Cardiovascular adverse reactions reported with INOCOR lactate injection include arrhythmia (3%) and hypotension (1.3%).

Hepatic toxicity: In dogs, at IV doses between 9 mg/kg/day and 32 mg/kg/day, amrinone showed dose-related hepatotoxicity manifested either as enzyme elevation or hepatic cell necrosis or both. Hepatotoxicity has been observed in man following long-term oral dosing and has been observed, in a limited experience (0.2%), following IV administration of amrinone.

Hypersensitivity: There have been reports of several apparent hypersensitivity reactions in patients treated with oral amrinone for about two weeks. Signs and symptoms were variable but included pericarditis, pleuritis, and ascites (one case); myositis with interstitial shadowing on chest x-ray and elevated sedimentation rate (one case); and vasculitis with nodular pulmonary densities, hypoxemia, and jaundice (one case). The first patient died, not necessarily of the possible reaction, while the last two resolved with discontinuation of therapy. None of the cases were rechallenged, so attribution to amrinone is not certain, but possible hypersensitivity reactions should be considered in any patient maintained for a prolonged period on amrinone.

General: Additional adverse reactions observed in intravenous amrinone clinical studies include fever (0.9%), chest pain (0.2%), and burning at the site of injection (0.2%).

MANAGEMENT OF ADVERSE REACTIONS *Platelet count reductions:* Asymptomatic platelet count reduction (to less than $150,000/mm^3$) may be reversed within one week of a decrease in drug dosage. Further, with no change in drug dosage, the count may stabilize at lower than predrug levels without any clinical sequelae. Predrug platelet counts and frequent platelet counts during therapy are recommended to assist in decisions regarding dosage modifications.

Should a platelet count less than $150,000/mm^3$ occur, the following actions may be considered:

- Maintain total daily dose unchanged, since in some cases counts have either stabilized or returned to pretreatment levels.
- Decrease total daily dose.
- Discontinue amrinone if, in the clinical judgment of the physician, risk exceeds the potential benefit.

Gastrointestinal side effects: While gastrointestinal side effects were seen infrequently with IV therapy, should severe or debilitating ones occur, the physician may wish to reduce dosage or discontinue the drug based on the usual benefit-to-risk considerations.

Hepatic toxicity: In clinical experience to date with IV administration, hepatotoxicity has rarely been observed. If acute marked alterations in liver enzymes occur together with clinical symptoms, suggesting an idiosyncratic hypersensitivity reaction, amrinone therapy should be promptly discontinued.

If less than marked enzyme alterations occur without clinical symptoms, these nonspecific changes should be evaluated on an individual basis. The clinician may wish to continue amrinone, reduce dosage, or discontinue the drug based on the usual benefit-to-risk considerations.

OVERDOSAGE Doses of INOCOR lactate injection may produce hypotension because of its vasodilator effect. If this occurs, amrinone administration should be reduced or discontinued. No specific antidote is known, but general measures for circulatory support should be taken.

HOW SUPPLIED Ampuls of 20 mL sterile, clear yellow solution containing INOCOR 5 mg/mL, box of 5 (NDC 0024-0888-20). Each 1 mL contains INOCOR lactate equivalent to 5 mg base and 0.25 mg sodium metabisulfite in Water for Injection. The pH of INOCOR lactate injection is adjusted to a range of 3.2 to 4.0 with lactic acid or sodium hydroxide.

Protect INOCOR lactate ampuls from light. Ampul packaging is light resistant for protection during storage.

Store at room temperature.

NOTE: Parenteral drug products should be inspected visually and should not be used if particulate matter or discoloration is observed.

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Dual-acting, energy-efficient

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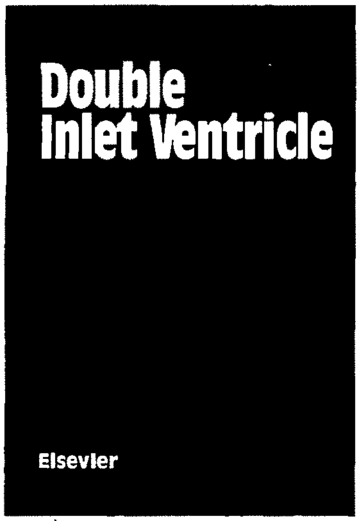

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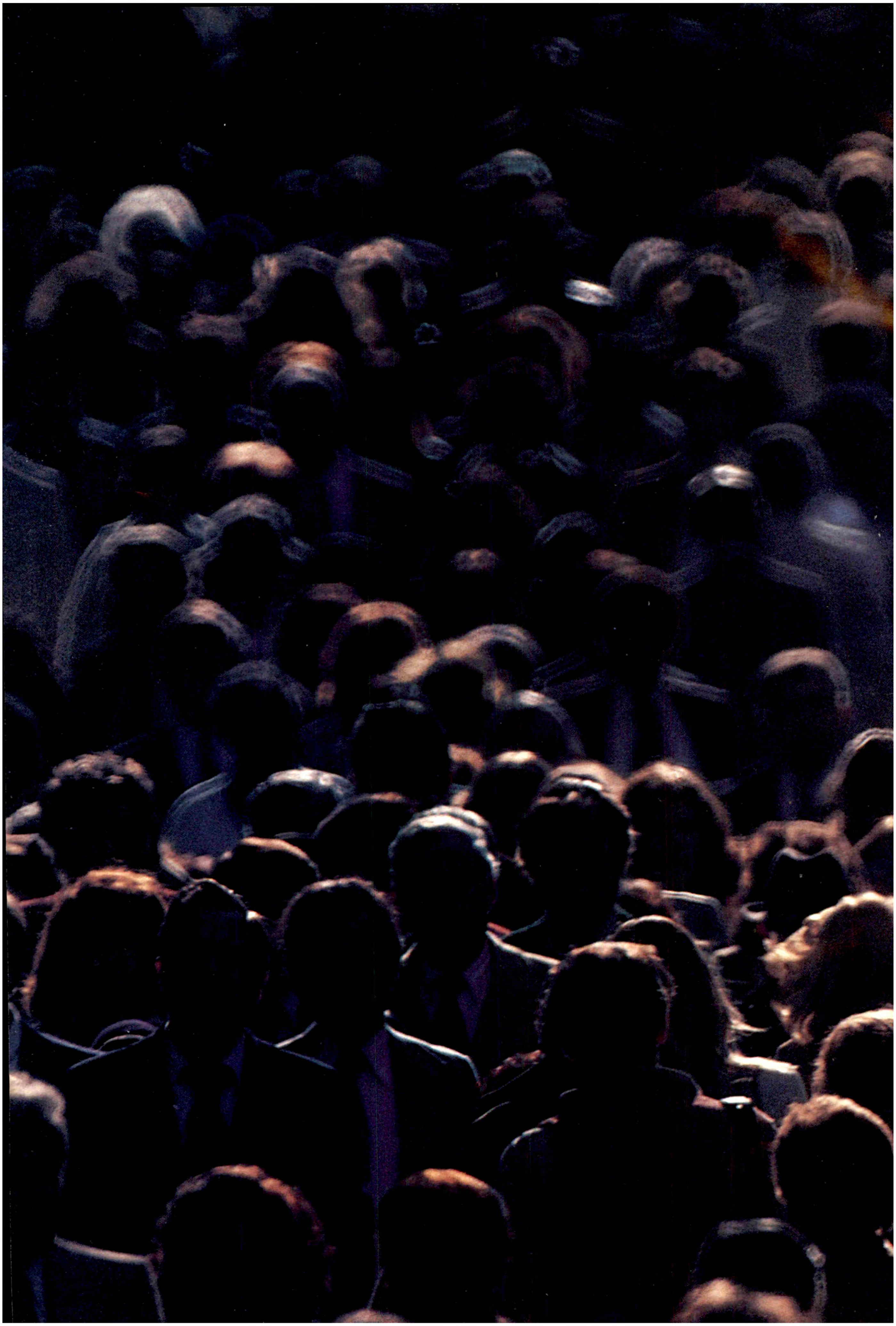

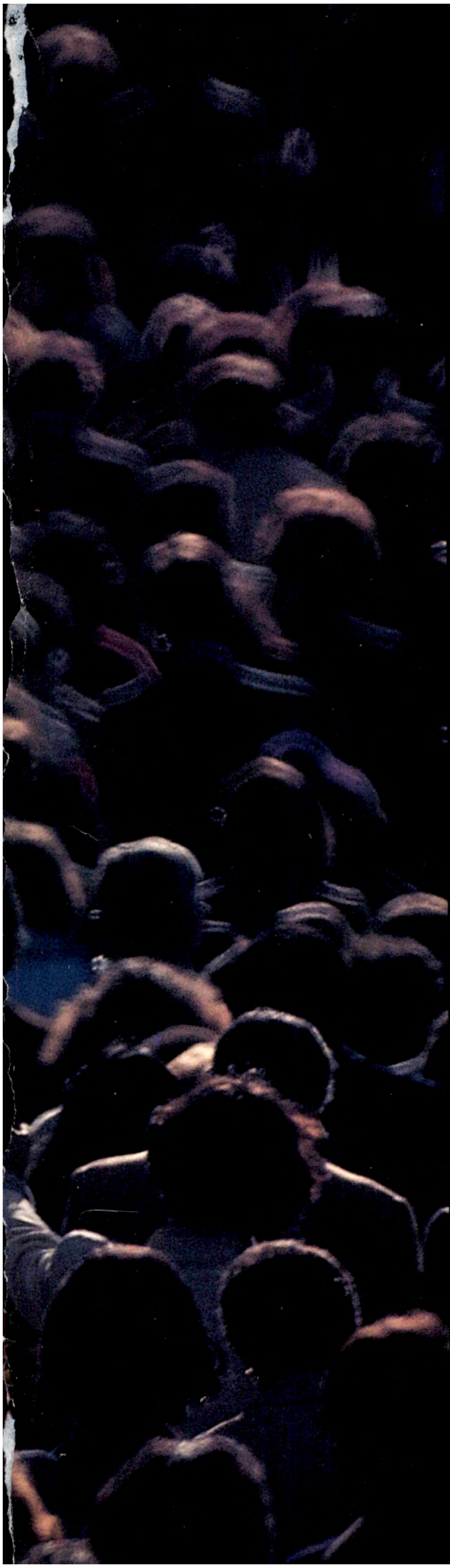

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